THE READINESS, NEED FOR, AND EFFECT OF MHEALTH INTERVENTIONS TO IMPROVE IMMUNIZATION TIMELINESS AND COVERAGE IN RURAL WESTERN KENYA

by
Dustin Gibson, MS

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Abstract

Background: As mobile phone ownership levels grow globally, opportunities to target hard-to-reach populations through mobile-health technologies become more realistic. In a rural Kenyan population, this dissertation seeks to assess the magnitude and risk factors of immunization timeliness and coverage, to determine the readiness of a community for mHealth interventions by assessing prevalence and risk factors for mobile phone ownership and SMS utilization, and to assess the effect of the Mobile Solutions for Immunization (M-SIMU) cluster randomized controlled trial.

Methods: A cross-sectional survey of Kenyan caregivers was conducted to collect baseline immunization and mobile phone ownership estimates for M-SIMU. Predictors of mobile phone ownership were obtained through multivariable logistic regression. Risk factors for delayed immunizations and not receiving immunization were calculated using binomial regression with log link. The M-SIMU trial randomized villages to four arms: Control, short message system (SMS) reminders only, SMS reminders + 75 Kenyan Schillings (KSH) incentive or, SMS reminders + 200 KSH incentive. Inverse Kaplan-Meier curves and Cox regressions assessed the intervention's effect on pentavalent3 and measles vaccination.

Results: Older maternal age, higher maternal literacy and education, smaller households, and higher socioeconomic status were associated with phone ownership. Immunization coverage for the third dose of pentavalent vaccine (pentavalent3), measles, and fully immunized children (FIC) were 95%, 83%, and 80%, respectively. Delayed pentavalent1 was associated with not receiving pentavalent3 (RR: 5.61; 95%CI: 3.77-8.33), measles

vaccine (RR: 1.51; 95%CI: 1.15-1.99), and FIC (RR: 1.87; 95%CI: 1.51-2.32). The prevalence of delayed pentavalent1, pentavalent3, and measles were 11%, 24%, and 29%, respectively. No common risk factors in the delay models were found. For M-SIMU, Kaplan-Meier curves found significant differences across arms in time to pentavalent3 ($p<0.01$) but not measles vaccination ($p=0.10$). SMS + 200 KSH infants were associated with pentavalent3 vaccination (HR: 3.33; 95%CI: 1.71-6.47) and approached significance for measles (HR: 2.05; 95%CI: 0.95-4.41; $p=0.07$), as compared to controls. The SMS only and SMS plus 75KSH were not significantly associated with either vaccine.

Conclusions: In a population with moderate phone ownership, high immunization coverage, and moderate vaccine delays, SMS reminders plus 200KSH improved pentavalent3 vaccination.

PhD Advisor: Dr. Daniel Salmon, Associate Professor
Department of International Health

Dissertation Readers: Dr. Alain Labrique, Associate Professor
Department of International Health

Dr. William Moss, Professor
Department of Epidemiology

Dr. David Bishai, Professor
Department of Population, Family, and Reproductive Health

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a hard-working colleague, and a great friend

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List of terms and abbreviations

AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
ACIP	Advisory Committee on Immunization Practices
BCG	Bacillus Calmette–Guérin vaccine
CAB	Community Advisory Board
CCT	Conditional Cash Transfer
CDC	Centers for Disease Control and Prevention
CHW	Community Health Worker
CI	Confidence Interval
CI	Community Interviewer
DHS	Demographic and Health Survey
DMOH	District Ministry of Health
DTP	Diphtheria, Tetanus, Pertussis antigens containing vaccine
DTP3	3 doses of DTP vaccine
DVI	Division of Vaccines and Immunization
EPI	Expanded Programme on Immunization
ERC	Ethical Review Committee
FGD	Focus Group Discussion
FIC	Fully Immunized Child
GAVI	Global Alliance for Vaccines
HDSS	Health and Demographic Surveillance System
HIV	Human immunodeficiency virus
HPV	Human Papillomavirus vaccine
HR	Hazards Ratio
KEPI	Kenyan Expanded Programme on Immunization
KEMRI	Kenya Medical Research Institute
KES	Kenyan Schilling
KSH	Kenyan Schilling
MCH	Maternal and child health
mHealth	Mobile-Health
mMoney	Mobile-Money

M-SIMU	Mobile Solutions for Immunization Trial
MICS	Multiple Indicator Cluster Survey
NGO	Non-governmental organization
PCV	Pneumococcal conjugate vaccine
Pentavalent3	3 doses of pentavalent vaccine
OR	Odds Ratio
RCT	Randomized Controlled Trial
RR	Risk Ratio
SES	Socio-economic status
SMS	Short Message System
SSC	Scientific Steering Committee
U5MR	Children under 5 mortality rate
USD	United States Dollar
VR	Village Reporter
WHO	World Health Organization

Chapter 1. Introduction

1.1 Executive summary

Approximately one in 13 children in Kenya and one in five children in our study site, the Gem District in western Kenya, will die before their 5th birthday, with the majority of deaths attributed to infectious diseases.[1,2] Many of these deaths are preventable by vaccination, yet many children in Kenya are not vaccinated or are vaccinated late.[3] The third dose of pentavalent vaccine (pentavalent3; containing vaccines for diphtheria, tetanus toxoid, pertussis, hepatitis B, and *Haemophilus influenzae* type b antigens) is scheduled to be given at 14 weeks of age[4] and is frequently used to assess the strength of a country's immunization system.[5,6] In our study site, 54% of infants received the third dose of pentavalent vaccine by 24 weeks of age in 2010. When measured at 12-23 months, the pentavalent3 coverage increases to 83%, suggesting both the need for efforts at increasing vaccine coverage and vaccine timeliness.

Measures of timely immunization are often omitted from immunization reporting systems, despite their importance. First, most mortality from vaccine preventable diseases occur early in childhood in developing countries[7-9]; ensuring vaccinations are given as early as possible will save lives. Second, timely vaccination ensures higher levels of herd immunity by reducing the pool of susceptible individuals, thereby protecting infants that are too young to be vaccinated from deadly vaccine-preventable diseases.[10]

Two demand-side interventions, short message system (SMS) reminders and small monetary incentives, have been shown to motivate positive health behaviors elsewhere.[11-16] However, the efficacy of SMS reminders to improve immunization

coverage in sub-Saharan Africa had neither been evaluated nor used in conjunction with monetary incentives until present. This 152 village randomized controlled trial called the Mobile Solutions for Immunizations (M-SIMU) will test whether SMS immunization reminders, either with or without mobile-phone based incentives, can improve timeliness and coverage of routine pediatric vaccines.

Critically, the success of our pilot study in a neighboring division, Karemo, showed that a mobile phone based system that delivers travel subsidies and SMS reminders is technically feasible and welcomed by the community.[17] The pilot study identified several lessons that were incorporated into the design of the M-SIMU randomized controlled trial.

Additionally, as part of M-SIMU's implementation, 2632 households were interviewed as part of the baseline survey in April of 2013 to ascertain immunization coverage and mobile phone ownership estimates. Furthermore, focus group discussions were conducted in June 2013, prior to M-SIMU enrollment, to receive both community feedback on mobile-health (mHealth) interventions and input on the study design. These focus group discussions, baseline survey, and a pilot analysis of the M-SIMU randomized controlled trial serve as the backbone of this dissertation.

Despite a lack of rigorous scientific evidence of effectiveness, mHealth and conditional cash transfer programs continue to spread throughout Africa.[18-21] Lessons learned from these studies will help in the effective design of similar programs and will assist decision makers in the Kenyan Ministry of Health, as well as those in other African countries, before committing the investment, time, and effort that will be necessary to scale-up these programs. Moreover, this project has the opportunity to assess the

potential of mobile phone technologies in achieving the Millennium Development Goal of reducing childhood mortality in Africa.

1.2 Study objectives

Primary Aim #1: To identify and compare predictors of immunization coverage and timeliness for third dose pentavalent vaccine, measles vaccine, and fully immunized[1] children in a rural Kenyan pediatric population

Primary Aim #2: To describe parents' perceptions of mHealth interventions targeting immunization coverage and to identify predictors of mobile phone ownership and SMS utilization in rural western Kenyan mothers

Primary Aim #3: To determine the effect of SMS reminders, with or without monetary incentives, on timeliness of pentavalent vaccine series and measles vaccine as compared to control infants in rural western Kenya

[1] Fully immunized children have received BCG, three doses of polio, three doses of pentavalent, and measles vaccines

1.3 Organization of the dissertation

This dissertation is presented in seven chapters. The first chapter provides an executive summary and primary aims. The second chapter is a substantive literature review of determinants of immunization coverage and timeliness, global and Kenyan-specific mobile phone ownership levels and their determinants, randomized controlled trials employing SMS reminders conducted in sub Saharan Africa, and studies utilizing incentives to promote positive behavior change. The third chapter details the study design and analyses conducted. Chapters four through six describe three scientific studies. Chapter four focuses on immunization coverage, timeliness, and their risk factors. Chapter five assesses the mobile-health landscape of rural western Kenyan by detailing the results of focus group discussions on mobile-health interventions to improve immunization and an examination of predictors of mobile phone ownership and SMS utilization. Chapter six describes the results of a pilot analysis of the Mobile Solutions for Immunization (M-SIMU) village randomized controlled trial. Lastly, chapter seven provides a summary of key findings from chapters four through six, discusses potential policy implications, and suggests future research agendas. Supplemental data, survey instruments used, and ethical approval forms are included in the appendix

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Chapter 2. Relevant Literature

2.1 Introduction

Few interventions available to public health practitioners rival the cost-effectiveness of vaccines when it comes to reducing childhood morbidity and mortality.[1] Recent 2013 estimates found that of approximately 6.3 million children died before their fifth birthday, with 51.8% (3.3 million) of these deaths attributed to infectious diseases. In regards to vaccine preventable diseases (VPDs), pneumonia (935,000 deaths) and diarrhea (578,000 deaths) were responsible for the most deaths.[2] Measles, pertussis, tetanus, and meningitis, four other vaccine preventable diseases, were responsible for 362,000 deaths in children under five years old.

Across the globe, numerous studies have identified risk factors for being unimmunized [3-5] and not receiving vaccinations in a timely manner.[6, 7] Identifying determinants of vaccination coverage and timeliness is important because it allows implementation of interventions aimed at those under- and un-immunized.[8-11] The scale-up of these interventions has the potential to save millions of lives across resource-constrained countries.[12]

Mobile-health (mHealth) is a burgeoning field due to exponential growth in mobile phone ownership, particularly in low-income countries.[13, 14] Although this field of study is in its infancy[15], mHealth technologies have been effective at promoting positive health behavior change.[16] Moreover, there is increasing recognition that mHealth technologies may have a role in improving immunization rates of traditionally hard-to-reach infants

through use of Short Message System (SMS) reminders[17], which target demand-side deficiencies in vaccine schedule knowledge and forgetfulness of immunization dates.

Small monetary incentives, or other valuable goods, that are conditioned on vaccine receipt, are another example of demand-side interventions that can be employed to improve immunization coverage. Although only a few rigorous studies on incentives exist, the results for improvements in timely vaccination rates are promising.[18, 19]

In this chapter, global and Kenya-specific determinants of immunization coverage and timeliness will be described, followed by a discussion of mobile phone ownership coverage levels and their predictors. A review of mHealth randomized controlled trials, particularly focusing on sub Saharan Africa and immunizations, ensues. Chapter 2 concludes with a summary of the evidence for small monetary incentives and their effect on health behavior change, including immunization.

2.2 Estimates of immunization coverage and timeliness

2.2.1 Estimates of immunization coverage

Vaccination is one of the most cost-effective interventions for increasing childhood survival.[1] Global estimates find that current immunization programs save over 2.5 million lives a year.[1] Despite the lifesaving potential of vaccines, in 2007 approximately 20% of children, or about 24 million infants, did not receive all the scheduled vaccines[1] and if they were immunized, they often received the vaccinations late.[7]

DTP3 coverage (3 doses of diphtheria, tetanus toxoid, and pertussis antigen containing vaccine) of children 12-23 months old is a common indicator of the strength of a country's immunization system to deliver vaccines.[20, 21] The DTP vaccine is globally

being replaced by the pentavalent vaccine, which includes DTP antigens plus hepatitis B, and *Haemophilus influenzae* type b antigens. DTP and pentavalent vaccines will be used interchangeably throughout the dissertation to broadly discuss immunization coverage. The DTP vaccine is recommended to be given when an infant is 6, 10, and 14 weeks old in accordance with the Expanded Programme on Immunization (EPI) schedule (Table 2.1).[22] In 2011, globally 83% of children ages 12-23 months received 3 doses of DTP[23]. These estimates are much lower for Africa and South East Asia, 71% and 75%, respectively.[23]

2.2.2 **Estimates of immunization timeliness**

An often overlooked aspect of DTP and other vaccine-specific estimates is the age group for which coverage is being assessed. Although the DTP series is to be completed by 14 weeks of age in most lower-income countries, DTP vaccination coverage is routinely measured in infants aged 12-23 months. The measurement at this time window does not capture any delays in vaccine administration.

Timeliness of vaccine receipt is important for two reasons. First, the diseases which pediatric vaccines protect against often have highest morbidities and mortalities at earlier stages of life. Delays of infant immunization have been associated with increased cases of pertussis[24, 25], hepatitis B[26], and *Haemophilus influenzae* type b.[27] Second, timely vaccination ensures maximal herd immunity[28], thereby protecting those that are too young to be vaccinated, are medically contraindicated, or do not produce a sufficient immunological response to vaccination. Herd immunity is dependent on the vaccine's ability to produce an protective immunological response in a sufficient proportion of the population to reduce transmission of disease. Delays in vaccination lessen population

coverage and create a pool of susceptible individuals thereby increasing the pathogen's ability to spread and potentially increasing the risk of exposure.

Although timely vaccination in more affluent countries has been studied for some time[29-33], this concept has only recently been applied to resource-constrained countries[6, 7] with many of these studies being published in 2012 and later. When timely immunization has been examined, vaccination delays have been found to be prevalent across lower income countries. Two systematic reviews identified a median delay of 6.2-6.3 weeks for DTP3 across 76 lower and middle-income countries (10 countries were replicated in both reviews).[6, 7] In one review, the median delay of the 75% percentile across 45 countries was 13.5 weeks.[7] National estimates of median delay for DTP3 in Kenya were lower, 3.2 weeks in 2003, but 25% of Kenyans had DTP3 delays greater than 7.5 weeks.[7] For our study site, Gem District Kenya, 2003 estimates found the median delay for DTP3 was greater than 10 weeks.[34]

Still, as global immunization coverage levels have markedly improved over the past decade [21, 35], the paradigm must shift from concerns about children being vaccinated, to ensuring vaccinations are given on time.

2.3 Predictors of immunization coverage and timeliness: global

2.3.1 Predictors of immunization coverage

The literature on predictors of vaccination coverage (i.e. receiving versus not receiving a vaccine) is abundant, especially when compared to that of vaccination timeliness (receiving a vaccine later than the recommended date). Like vaccine timeliness, vaccination coverage is dependent on contextual factors that may be specific to its respective population. In an analysis of Demographic and Health Survey (DHS)

immunization data from 26 sub Saharan African countries representing 27,094 children and 8,546 communities, the authors found that 32% and 21% of the variance in non-vaccinated children was attributable to community and country-level variables, respectfully. Maternal and paternal education, were strongly associated with non-immunized children, (OR: 1.35, 95%CI 1.18 to 1.53) and (OR: 1.13, 95%CI 1.12 to 1.40), respectively. Maternal access to media (OR: 0.94, 95%CI 0.94 to 0.99) and maternal care-seeking behaviors (OR: 0.56, 95%CI 0.54 to 0.58) were found to be protective for non-immunization.[3]

Because of the high dependence on community- and country-level factors, a broad discussion on potential determinants of immunization coverage is recommended and will later be followed with Kenya-specific findings. Guiding this discussion of 'global predictors' will be a recent systematic review that classified these determinants into four broad categories: immunization systems, communication and information, family characteristics, and parental attitudes.[4] Overall, this review encompasses 202 articles describing studies conducted in 51 unique countries. The results from this systematic review will serve as a guideline for discussion of potential determinants of immunization and not be used to draw conclusions about the importance and strength of the socio-demographic variable's associations with immunization status.

A. *Immunization systems*

The most commonly reported associations with immunization coverage were deficiencies in immunization systems. Immunization systems included long distances from and poor access to vaccination clinic, costs associated with vaccination, rural residence, health worker knowledge, and missed opportunities to vaccinate.[4]

Distance from the clinic has long been recognized as an important determinant of healthcare utilization, including vaccination.[36-40] The so-called "distance decay effect" posits that the rate of utilization varies inversely with distance".[41] A recent systematic review and meta-analysis (manuscript in preparation by this dissertation's author) found that this distant decay effect was observable in immunization, antenatal care, postnatal care, antenatal immunization with tetanus toxoid, delivery at a health facility or by a skilled birth attendant, and healthcare seeking for illness outcomes.[42]

In this review, three main vaccination status outcomes were evaluated - completion of the full Expanded Programme on Immunization sequence (birth dose of BCG, three doses of DTP and polio, and one dose of measles vaccine)[43-58], completion of DTP3/Pentavalent3[59-63], and BCG vaccination.[45, 59, 61, 64, 65] Of the 21 studies examining full immunization status or DTP3/Penta3 completion as compared to incomplete and/or no immunization, 14 (66.7%) found a significant distance decay effect. Similar findings were seen for analyses that adjusted for potential confounders; 12/17 studies (70.6%) found a distance-decay effect. A significant dose-response effect of decreased immunization status with increasing distance was observed in three (42.9%) of seven studies that had multiple distance intervals.[46, 50-52, 54, 56, 57] Additionally, significant distance decay effects were also found in three (60%) of five BCG immunization outcomes.

In meta-analysis (Figure 2.1), the pooled summary estimates from six studies found that infants living greater one kilometer were significantly less likely to be completely immunized than infants living within one kilometer from a health facility [pooled OR (pOR): 0.61; 95% CI (0.45-0.82), I^2=85%][46, 51, 53-55, 63], as were infants living

greater than two kilometers compared with those living within to two kilometers from a health facility in three studies [pOR: 0.64; 95% CI (0.43-0.94), I^2=73%].[44, 51, 56] No significant distance decay effect was found between those living greater than five kilometers from a health facility versus those within five kilometers in three studies [pOR: 0.55; 95% CI (0.27-1.12), I^2=71%].[48, 56, 59] The pooled estimate trended towards the suggestion of a distance decay effect and was likely underpowered.

B. *Family Characteristics*

Family characteristics were the second most frequently cited reason for under-immunization in resource-constrained countries.[4] The most common subcategory was low maternal education.[4] Gem District, Kenya 2003 cross-sectional survey results corroborate the systematic review's finding of low maternal education (OR=0.32; 95%CI: 0.12-0.86) and also found that higher numbers of children in the household (OR=0.24; 95%CI: 0.11-0.53) are associated with incomplete immunization.[34]

The second most commonly cited reason within family characteristics was lower socio-economic status.[4] Implicit with long distances from health facility are indirect and direct costs associated with transportation which for lower income families poses a significant burden or barrier. As a result, families either walk long distances to the health facility or do not seek care.[66, 67]

C. *Parental attitudes and knowledge*

The third category of reasons for under-immunization is parental attitudes and knowledge. Parental attitudes and vaccination knowledge accounted for 22% of reasons for underimmunization in developing countries[4]. The most common subgroupings were a

lack of knowledge that vaccinations prevent disease, belief that vaccinations cause harm or are not effective, and lack of motivation.[4]

These determinants represent demand side deficiencies that are both infrequently acknowledged and targeted to increase immunization coverage[68], but have found to be effective when interventions addressing these deficiencies were implemented. A randomized cluster controlled trial in Pakistan found that three community discussions over a span of seven months tripled the odds of DTP3 immunization in children ages 12-23 months (OR= 3.36; 95%CI: 2.03-5.56).[69] In Ghana, a cluster randomized controlled trial showed that study staff visiting homes and providing vaccination reminders statistically increased full immunization coverage by 20%.[70]

2.3.2 **Predictors of immunization delay**

Two reviews examined the determinants associated with DTP3 vaccination delays from Demographic and Health Surveys (DHS) in 45 countries and Multiple Indicator Cluster Surveys (MICS) from 31 low income countries.[6, 7] Several predictors of DTP3 delays from adjusted models were significant in both reviews, such as higher number of children in the household, rural residence, and younger mothers. Findings were inconclusive for gender as a determinant of timely DTP3; male children were more likely to experience delays in the MICS review but gender was non-significant in the DHS review.[6, 7] One review found that children being born at home and lower maternal education were significant predictors of delay.[7] Lastly, of all determinants examined in both reviews, the poorest households had the highest odds of delayed vaccination (OR=2.08; 95%CI: 1.94-2.08).[6] This finding hints at the potential of monetary incentives as a catalyst for increasing vaccine timeliness.

In addition to these two reviews of national survey data, there is a growing body of literature for study site-specific predictors of vaccination delays in lower income countries[71-84],with many of these studies being published in 2012 and later. These studies have been conducted in a range of countries including Ghana[75, 77], Uganda[71, 85], Tanzania[78], Burkina Faso[80, 82], Nigeria[79, 81], South Africa[74], India[72], China[76], and Bangladesh.[84]

Three studies have examined determinants of delayed vaccination for the full EPI schedule (BCG, DTP, polio, and measles) in developing countries.[71, 74, 85] Analyses that adjusted for potential confounders found that giving birth at home[71, 74], increasing numbers of children in household[71, 74], lowest wealth quintile[71], unmarried mothers[71], and low maternal education[85] were significant predictors of a child's timely full immunization status.

In addition to studies examining risk factors for delays in FIC, there are two studies that have looked at delays in the administration of pentavalent3.[78, 82] In both studies, lower socioeconomic status was associated with delayed pentavalent3.[78, 82] Lower maternal education and higher number of siblings were associated in one study.[82]

Predictors of delay for full immunization status and DTP3 may differ due to the inclusion of measles vaccine in full EPI immunization analyses. At younger ages infants visit health facilities for wellness checkups and immunizations, typically at 6, 10, and 14 weeks of age. Prior to measles vaccination at 9 months of age, there are no other scheduled visits. Because of the long duration between the immunization visit at 14 weeks of age and measles, it is likely there is a higher chance of mother's forgetting

about the measles appointment. Still, as discussed above, there is some overlap in full immunization and DTP3 coverage delay determinants.

2.4 Predictors of immunization coverage and timeliness: Kenya

2.4.1 Predictors of immunization coverage:

Over the past 25 years, numerous studies have reported Kenyan immunization coverage estimates and their associations with socio-demographic variables.[34, 86-93] In these analyses, higher levels of maternal education[34, 86, 87, 90, 92] and lower number of children in the household[34, 87, 90, 91, 93] are consistently associated with higher immunization coverage levels. Yet, because these studies were conducted across a range of settings, including urban[87, 88, 90, 92] and coastal areas[89, 91], differences in primary immunization outcomes ranging from pentavalent3 coverage to fully immunized children, and a lack of uniformity in socio-demographic variables included in analyses across all studies, it should be expected that predictors of immunization coverage are not uniform.

Moreover, it is possible that predictors of immunization coverage have changed over time as more Kenyan infants are being vaccinated. Data from successive Kenyan Demographic and Health Surveys (DHS) found improvements in DTP3 coverage from 2003, 72%, to 2009, 86%.[94] Study site specific estimates for Gem District, Nyanza Province, Kenya found DTP3 and measles coverage estimates, respectively, to be 68% and 50% in 2003[34] and 95% and 84% in 2011.[93] The gains in immunization coverage are likely tied to the heightened awareness and global efforts of improving immunization systems ([95, 96])

To illustrate a temporal change in predictors of immunization coverage, a recent analysis from our study site found that the quality of interaction with community health workers (CHW) and the frequency of interaction were significant factors affecting FIC coverage.[93] Recently, Kenya has integrated community health workers (CHW) into Kenyan national policy to improve the health of children and mothers.[97] As part of their job duties, CHWs trace infants that have defaulted on their immunizations and refer them to the clinic. The CHW successful referral of infants for vaccination may override some of the traditional risk factors for not bringing infants for vaccination.

The most recent analysis of determinants of immunization status from this dissertation's study area occurred in September 2011[93], though the geographic scope of this cross-sectional survey is much larger than the dissertation study area. This analysis surveyed mothers from Siaya, Ugenya, Kisumu West, and Gem Districts. The dissertation study area is confined to Gem District. Results from multivariate logistic regression found that average (OR: 2.69; 95%CI: 2.02–3.60) and high knowledge of vaccination schedule (OR: 8.12; 95%CI: 5.51–11.98) were significantly associated with fully immunized child coverage. Long birth intervals (OR: 1.85; 95%CI: 1.10–3.09), first born children (OR: 2.15; 95%CI: 1.20–3.84), and lower numbers of children under five years old in the household (OR: 1.40; 95%CI: 1.04–1.88) were also significantly associated with full immunization. As discussed above, the investigators also measured the effect of CHW performance, a composite measure of quality and frequency of interactions. Infants that had high levels of CHW performance had two-fold higher odds of being fully immunized than infants that had poor levels of CHW performance (OR: 2.20; 95%CI: 1.40–3.47).

As global and Kenyan-specific immunization coverage levels have improved over the past decade, it is likely that predictors of immunization status may also change. Risk factor analyses to determine socio-demographic variables associated with infants not being vaccinated are useful because they can identify particular subsets of the population to target public health interventions that improve immunization coverage. When possible, analyses should include individual- and community-level variables in risk factor analyses to account for variation within individuals and their surroundings.

2.4.2 **Predictors of immunization delay: Kenya**

In regards to predictors of immunization delay in Kenya, three studies have examined distribution of immunization delays and determinants. Two of these studies were conducted in a coastal city, Kilifi[89, 91], and the other was an analysis of 2003 data from this dissertation's study area.[34] The two studies from Kilifi both used inverse Kaplan Meir curves and Cox Proportional Hazard Models to obtain estimates for predictors of pentavalent vaccination. In one model, seasonality was the only predictor of timely immunization. The authors found that infants with vaccination due during the rainy season were less likely to be timely immunized than those with vaccination due dates during the dry season (HR=0.86, 95% CI: 0.81–0.92).[89] Bivariate analyses found that maternal education and migrant status were significantly associated with timely immunization, but that this effect disappeared in adjusted analyses. Distance to the clinic and travel time was not significant in both bivariate and multivariate analyses.

In the other Kilifi-based study, and similar to the previous results reported, rainy season was also predictive of timely pentavalent immunization, (HR=0.73, 95% CI: 0.61–0.89).[91] Unlike the previous study, the authors found that distance to the clinic was

predictive of timely immunization, although the effect size was modest (HR=0.95, 95% CI: 0.91–1.00). Additionally, an increasing number of children in the family were found to be predictive of immunization delays.

Overall, the research on immunization delays in Kenya is limited in both scope and depth, particularly from this dissertation's study site. The identification of risk factors and determinants of delayed immunization is important so that interventions and health programs can target particular subsets of the population to attempt to improve timely immunization coverage estimates. Chapter four of the dissertation discusses the findings from a large cross-sectional survey that aims to assess risk factors of immunization coverage and timeliness.

2.5 Mobile phone ownership

Globally, the number of people owning mobile phones grew from 1 billion in 2000 to 6 billion in 2012.[14] The predominant driver of this growth was mobile phone adoption by lower income countries. In 2010, 77% of mobile phones are located in developing countries, contrasted to only 22% in 2000.[14] Particularly, the use of mobile phones has skyrocketed in Africa, with Kenya viewed as a pioneering country. In 2005, 12% of Africans were mobile phone subscribers. This estimate tripled to 37% in 2009 and population coverage, the percentage of inhabitants within a cellular signal, reached 81%.[13] In Kenya, September 2011 estimates reveal over 26 million cellular subscriptions, equating to a 20.4% increase from the previous year and resulting in 67% of the adult population as mobile phone subscribers.[98] Approximately two-thirds of subscriptions are with the mobile provider Safaricom. The other three mobile networks

operating within Kenya are Airtel, Essar Telecom (Yu), and Telkom Orange, with market shares, respectively, of 15.7%, 10.4%, and 6.2%.[98]

Mobile phone usage and ownership levels have globally risen, yet a noticeable lack of data on sub-national levels of population coverage exists. Nyanza Province, the site of the proposed study, observed that 69% of *households* possess a mobile phone in 2009.[99] Similarly, 70.9% of 72 households owned mobile phones in our 2011 pilot study.[100] Our empirical ownership findings are consistent with national data where 85% of Kenyans reported using a mobile phone, but only 44% reported owning one one.[101] In this national analysis, the authors found that high education levels, English literacy and gender were significant predictors of phone ownership.[101]

Gender gaps in phone ownership pervade and their existence may impede the delivery of mHealth interventions targeting women and children. In Kenya, sub-Saharan Africa, and South Asia, women are, respectively, 22%, 23% and 37% less likely (relative) than men to own a mobile phone.[102] In Nyanza Province, Kenya, women are 12% relatively less likely to own a mobile phone than men, with 65% of men and 57% of women owning a mobile phone.[99] The presence of low mobile phone ownership levels, coupled with a documented gender gap, will require novel solutions to maximize the reach of mHealth interventions.

Mobile phone ownership among women is not uniform. Globally, wealthier, more educated, city-dwelling, and younger women are most likely to own mobile phones.[102] Several studies have examined determinants of mobile phone ownership in Kenya.[101, 103] However, data on determinants specific to phone ownership in women is lacking, but is likely similar to global determinants.

In a recent analysis of 1,167 caretakers presenting to a health facility, 82% of which were women, analyses found that higher levels of education, male gender, lower poverty index scores, and urban dwelling were significant of mobile phone ownership.[103] Critically, there was no stratification of results by gender, making it difficult to assess determinants for mobile phone ownership in women.

It is imperative to study the distribution of mobile phone ownership in women across different socio-demographic strata. The findings that older as compared to younger, more educated as compared to least educated, wealthier as compared to poorer women were more likely to own a mobile phone should give pause to program implementers that seek to address health disparities through mobile-health interventions. Historically, these predictors of mobile phone ownership are often similar to predictors of healthcare utilization. Less educated, younger, impoverished women are individuals that would most likely benefit from mHealth interventions such as text message reminders, yet low levels of phone ownership complicates the delivery and receipt of intervention. In areas with low mobile phone ownership levels, mobile health interventions could be distributed to the phones of husband's or other household members as the majority of women, despite not owning, have access to a mobile phone.[101]

Lastly, in addition to low mobile phone ownership amongst females, a common critique of conducting mHealth interventions within Kenya is the country's high penetration of mobile phones may prevent the study results from being generalizable or replicable to other parts of Africa. The merits of this argument are discounted in two ways. First, as described above, the low levels of mobile phone ownership among Kenyan women will require novel approaches to target this audience and are likely

similar to approaches that could be applied in other countries. Second, although not all sub-Saharan countries have mobile phone ownership levels similar to Kenya, the rates of adoption over time are similar (Figure 2.2); characterized by low levels of adoption for several years and followed by exponential growth. As countries progress through this 'mobile phone transition', more and more countries will likely exhibit a similar mobile phone profile to Kenya.

2.6 mHealth and SMS reminders

Mobile phone applications have been used successfully for a variety of public health applications[104-106], referred to broadly as "mHealth." These applications include raising HIV awareness and treatment[107-109], remote data collection[110, 111], monitoring and disease outbreak tracking[112-114], health worker training[115-117], and diagnostics[118], to name a few. As mobile phone ownership levels continue to rise in lower income countries, mHealth solutions become more realistic.[15]

One of the most commonly employed applications of mHealth is the use of short message system (SMS; i.e. text messages) to promote a positive health behavior. The mechanism by which reminder messages encourage behavior changes can be viewed in terms of the Health Belief Model (Figure 2.3).[119, 120] First, reminder messages serve as a behavioral cue to prompt a health behavior. Second, they lower perceived barriers to accessing services and reduce the threshold for completing health behaviors. Reminders have been successful at increasing several forms of healthcare utilization[121-124] and have been delivered through several mediums including household members or health workers[70, 125], reminder cards delivered through postal mail[126-128], telephone calls[127, 129], e-mail messages[130, 131], and more recently, SMS messages.[107, 122, 132]

The impact of reminder messages in higher income countries is well documented. A systematic review of 49 studies that used various forms of patient reminder and recall interventions for immunizations found that these interventions increased immunization rates by 5-20%[9], although no studies were included from lower income countries. With strong evidence demonstrating the efficacy of reminders, the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP) recommended that reminder and/or recall systems be enacted to increase vaccination rates in the United States.[133]

Although postal and email reminders may work in higher income countries, the limited access to such commodities in rural Kenya hinders their implementation. However, the rise in mobile phone penetration both within Kenya and across lower income countries provides an alternative delivery avenue through use of SMS.

The scientific literature supporting the effectiveness of SMS reminders to enact positive changes across a variety of unique forms of healthcare utilization within higher income countries is abundant.[121-123] Specifically, two systematic reviews and meta-analyses concluded that SMS reminders improved rates of attendance at clinical appointments [(RR= 1.10; 95%CI: 1.02-1.19)[121] and (OR=1.48; 95%CI: 1.23-1.72)].[122]

2.6.1 **SMS reminders in Sub Saharan Africa**

The scientific evidence for SMS reminder interventions in Africa is modest, but slowly growing. As of August 2014, nine studies conducted in sub Saharan Africa (Table 2.2) randomized SMS reminders, with the majority showing a positive effect, as compared to a control group, on the healthcare utilization outcome under study.[107, 109, 116, 134-139] These outcomes included HIV treatment adherence (n=3)[107, 109, 137], HIV testing[134],

treatment of pediatric malaria[116], antenatal care attendance[136], institutional delivery[135], and post-circumcision clinic attendance.[138, 139] A meta-analysis of two Kenyan studies found a lower risk of non-adherence to antiretroviral medications at 48-52 weeks in those randomized to weekly SMS reminders; (RR 0.78, 95% CI 0.68-0.89).[124] Brief discussions for several of the studies will highlight lessons learned and points to consider with SMS reminder interventions.

One study conducted in Nairobi, Kenya found that HIV+ patients who received weekly SMS messages were less likely to report being non-adherent, defined as < 95% of ART doses over 3 months, (RR=0.81, 95% CI: 0.69-0.94) and less likely to have virologic failure at 12 months follow-up (RR=0.84; 95% CI: 0.71-0.99) than those not receiving SMS messages.[107] An additional study set in rural Nyanza Province, Kenya found similar improvements in adherence to those randomized to weekly SMS reminders (13% -16% difference mean difference), but no difference in those randomized to daily messages[109]; suggesting that a habituation effect may exist.

While the previous study showed a habituation effect to daily reminders sent for 48 weeks, a study set in South Africa found a frequency threshold may need to be reached in order to achieve an impact. In this study, 2533 participants were randomized to either a control group or one of four intervention arms. The interventions arms received either 3 or 10 SMS messages, of which their wording was either motivational or informational in aiming to increase HIV testing. The authors found significant uptake of HIV testing to those randomized to 10 motivational SMS reminders as compared to controls (OR =1.70; 95% 1.19–2.44), while the other three interventions (short form + info, short form + motivational, and long form + informational) were not significant.[134]

Equally as important, this study emphasizes that, and despite its intuitiveness, frequency and content of SMS messages are important in producing behavior change and, when considering the studies described previously, there is a fine balance between sensitizing SMS recipients and sending too few messages. Moreover, successful outcomes may hinge on appropriate phrasing of messages. This 'habituation-minimum threshold' balance may be dependent on the form of healthcare utilization (e.g. treatment versus prevention) the SMS messages aim to promote.

In the three previous trials, SMSs were targeted to health care seekers. In a recent Kenyan trial, community health workers were randomized to either control or intervention arms. Community health workers in the intervention arm received bi-daily text messages on case management for pediatric malaria. The messages were sent Monday through Friday for six months. The authors found that SMS reminders sent to health workers improved artemether-lumefantrine management of pediatric malaria by 23.7% (95%CI 7.6-40.0; p=0·004) immediately after intervention and that this effect persisted for 6 months after cessation of text messages (24.5%; 95%CI: 8.1- 41.0; 0.003)[116]. Despite the seemingly high number of SMS messages sent, 18 of 24 health workers interviewed were happy with the frequency of messages while 6 health workers thought that high frequency of reminders received would eventually induce boredom.[140]

2.6.2 **SMS reminders and immunizations**

In regards to SMS reminders and immunizations, there are no randomized controlled trials using SMS reminders in Africa. However, several randomized controlled trials conducted in lower-income, high-minority concentration neighborhoods of New York City found SMS reminders increase multiple types of vaccine coverage.[141-

[144] The first trial found that SMS reminders sent weekly for 5 weeks led to a 3.7% difference (95%CI: 1.5 to 5.9) in seasonal flu vaccine coverage in children ages 6 months to 18 years old. Subgroup analyses found that flu vaccine coverage increases were highest in children aged 6 to 23 months (6.2; 95%CI: 1.9%-10.5%).[143] Another study sent weekly SMS reminders to mothers of girls 9-20 years old 3 weeks before their daughter's next scheduled HPV vaccine dose. Girls in the SMS reminder arm were nearly twice more likely to receive their next dose of HPV within one month of scheduled date than those not receiving SMS reminders, (AOR: 2.03, 95%CI 1.29–3.22).[141]

The theoretical underpinning of SMS reminders, as described above, is grounded in the Health Belief Model. To improve immunization coverage, there are several points within health systems that could be intervened upon (Figure 2.4).[8] The three main intervention points are at the provider level, enhancing access to immunizations, and increasing community and individual demand for vaccination. Examples of provider level interventions include electronic immunization tracking systems[145, 146] and pay-for performance schemes[147, 148], where providers are paid small incentives for services delivered. Interventions that enhance access to vaccination include increasing cold chain capacity and vaccine procurement. Demand side interventions target healthcare seekers to increase the likelihood they are immunized. These interventions could target misperceptions and fears of vaccination or forgetfulness of the infant's immunization appointment. If either forgetting a child's immunization appointment or not knowing the vaccine schedule is the main reasons for infants not being vaccinated, or being vaccinated

late, SMS reminders that provide information on where and when the child is due for vaccination could improve timely immunization coverage.

With evidence that reminder messages and small incentives increase various forms of healthcare utilization[18, 19, 107, 109, 124, 149], we conducted a study in 2011 to test the feasibility of using a mobile phone based system to deliver SMS reminders and monetary incentives to increase vaccine coverage and timeliness in rural western Kenya.[100] Mothers were enrolled if they owned a mobile phone (26%) or had immediate access to one (74%). All mothers approached were able to identify a mobile phone to receive SMS reminders and incentives.

In this study, 72 mothers were sent SMS messages reminding them of their infant's pentavalent vaccination 3 days before, and on the date of, scheduled vaccination date. Mothers were also randomized to receive either $2USD worth of airtime or mobile money if they brought their child for vaccination within 4 weeks of the first and second dose of pentavalent vaccine.

Several lessons were learned from this feasibility study that benefitted the design of the M-SIMU cluster randomized control trial (Dissertation Chapter 6). Coding glitches in the software that automatically sends SMS messages based on the child's birth date were identified. We also encountered some hesitation from parents, particularly husbands, in enrolling their child for the study. For the RCT, the coding algorithms have been addressed and extensive community mobilization occurred to inform the population that these are not experimental vaccines.

Despite minor technical problems in the execution of the feasibility study, the results were promising. Approximately 57% of pentavalent doses were given on the scheduled date and 88% of pentavalent doses given within 3 days of scheduled date (Figure 2.5). Although there was no control group built into this study, SMS reminders were not delivered correctly to all participants. In as-treated analyses, pentavalent2 coverage was 95% for the 42 participants who received SMS reminders and whose vaccination status could be ascertained compared to 60% coverage for the 20 individuals who did not receive SMS reminders and whose vaccine status was ascertained. The small sample size and lack of a natural comparison group prevents drawing conclusions about the effectiveness of SMS reminders and CCTs to improve vaccine coverage and timeliness, but does suggest that SMS reminders, with incentives, may be effective at promoting timely immunizations in Kenya.[100]

There is much promise for SMS reminders to increase vaccination coverage, yet several limitations may inhibit their successful implantation. First, an implicit component of SMS interventions is the need for a literate population to guarantee that the intended reminders are being understood. In Nyanza Province, our study location, literacy levels approach 90% in women ages 15-49 years old.[94] However, a low literacy level is not an absolute contraindication for SMS usage; tools are being developed to assist illiterate populations.[150] Voice messages and/or use of pictures combined with training could circumvent this issue in other illiterate populations. Second, the effectiveness of SMS reminders is contingent on a population's access to mobile phones. A 2009 national analysis of Kenyan mobile phone ownership found that despite 45% of the population owning a mobile phone, 85% of Kenyans had access to one.[101] Sending

SMS reminders to populations with low mobile phone ownership levels will require novel solutions, such as sending text messages to friends and relatives of the intended recipient and relying on these individuals to relay the content of the SMS. Lastly, even if individuals own a mobile phone, the delivery of SMS reminders may not be effective because the phone is not charged, there is no mobile phone network, or individuals have changed their phone number.

In conclusion, SMS reminders have been modestly effective at enacting positive health behavior change across a range of health seeking behaviors in sub Saharan Africa.[107, 109, 116, 134-139] Although no study has examined the efficacy of SMS reminders on vaccination coverage within resource constrained settings, several trials conducted within the United States yielded positive gains in immunization coverage.[141-144] Qualitative studies have found that care takers in Nigeria and Burkina Faso would welcome SMS reminders for vaccination appointments and that they believe these reminders would be effective.[151, 152] Still, more scientific studies conducted in resource-constrained settings are needed before making policy recommendations.

2.7 Incentives for healthcare utilization

2.7.1 Conditional cash transfers

As described above, long distances to health facility and low socio-economic status are barriers to full immunization coverage. Lower income families balance the direct and opportunity costs of seeking healthcare with the perceived benefits of curative and preventive services. One potential solution is conditional cash transfers (CCTs) and/or incentives. A CCT is the transfer of money or other remunerable good for

completion of a positive behavior and are classically associated with poverty alleviation schemes and social-welfare programs.[149, 153] These positive behaviors can be non-health related (e.g. school attendance) or health-related, such as giving birth at a facility, returning for HIV test results, or immunization. Demand-side incentives are similar to CCTs in that remuneration is provided for completing positive behaviors, but differ in that incentives are of smaller value amounts.

CCTs, employed most notably in Latin and South America, have increased utilization of healthcare, improved nutritional indicators, and enhanced uptake of immunizations.[149, 154, 155] Importantly, CCT programs typically set the condition for transfer on broader behaviors (e.g. child wellness visits or school attendance) and then assess its effect both on the conditioned behavior and other indirect health indicators.[149] Moreover, and much like mHealth interventions, CCT programs are implemented before rigorous testing and assessed afterwards through program evaluations.[156]

The effect of CCTs on immunization coverage is mixed. A Honduran study observed a 6.9% increase in first dose of infant DTP coverage but no effect on measles coverage in those randomized to receive monthly vouchers conditioned on school attendance or well visits.[157] The effect may have been dampened as a result of the long lag between vaccination dates (DTP at 6 weeks, measles at 9 months) and age of assessment, 3 years old. In Columbia, households received a monthly average of $50 USD conditioned on school attendance and preventive healthcare visits. The program evaluation found the CCT improved probability of DTP3 completion in infants less than 24 months old.[158] Although estimates for a Nicaraguan cash transfer study, $ 25 USD per

month, found no effect on full immunization coverage in infants 12-23 months, the point estimate trended towards effect.[159]

2.7.2 **Demand-side incentives**

There is substantial evidence that small incentives can produce positive behavior change across a range of health behaviors in developed countries[160-162], which includes strong evidence for adult immunizations[161], with insufficient evidence for pediatric[163, 164] and adolescent vaccines.[165] Yet the literature on incentivizing immunizations in lower income countries is sparser than the evidence from both developed countries and conditional cash transfers. Although the evidence on provision of demand-side incentives directly conditioned on vaccine receipt in resource constrained settings is limited, their effect is more definitive and robust. Although incentives have not been tested in Kenya, Pakistani and Indian studies each found demand-side incentives improve immunization coverage. A cluster-randomized controlled trial was conducted in poor communities with low baseline immunization coverage levels in rural India. The authors randomized villages to one of three arms; control group, monthly immunization camps, and monthly immunization camps + an incentive of lentils for completion of each dose and metal plates for being fully immunized. The researchers found that providing incentives with immunization camps had large positive effects on full immunization coverage (mean % difference, 34%; RR=6.66; 95%CI: 4.53-8.80) and the effect was greater than immunization camps alone (mean % difference, 21%; RR=2.16; 95%CI: 1.54-2.78).[18] In Pakistan, two cohorts were used to assess whether providing food/medicine vouchers worth 2 USD for completion of each dose of DTP vaccine increased DTP3 coverage. Families that received vouchers had 2 times higher probability

of DTP3 completion than the cohort that did not receive incentives. (RR=2.20 95% CI: 1.95-2.48).[19]

An important consideration in incentivizing healthcare utilization is the determination of the incentive amount. The incentive needs to be sufficient to tip the mother's cost-benefit analysis towards bringing their child to the clinic, but not be excessive. High incentive amounts may inhibit the scalability and sustainability of a program and potentially distort the local economy. Additionally, there may be marginal gains in healthcare utilization if an incentive threshold exists.

Work in rural Malawi addressed this concern of incentive amounts and gains in healthcare utilization. Individuals were randomized to vouchers ranging from $0 to 3 USD that were redeemable if HIV test results were obtained.[166] The authors found that very small incentives (e.g. <$1.00) induced high uptake of HIV test results (>90%) and that there is marginal gains in testing uptake with increasing incentives beyond $1.00. Moreover, the effectiveness of incentives was greater in those living farther than 1.5 kilometers from the testing site. This suggests that in rural Africa, incentives that only cover part or all of transport costs might be successful, at least for HIV testing, and there may be a threshold to gains from incentives.

In addition to the Malawi study that randomized incentive amounts to determine if there was a dose response with the amount of the incentive and retrieving HIV test results, work from rural Kenya examined this phenomenon with voluntary male circumcision.[167] In this study, uncircumcised males were randomized to receive one of four study arms. The study arms were: (1) Control group where participants received standard of care and no incentive; (2) 200 KES incentive (85KES= 1USD); (3) 700 KES

incentive; and (4) 1200 KES. The incentives amounts were chosen to reflect transportation costs (200 KES) plus either one day's wage (500 KES) or two day's wage (1000 KES). Participants received the incentive if they were circumcised within two months. Adjusted analyses found that participants randomized to the 700 KES (OR: 4.3; 95%CI 1.7-10.1) and 1200 KES arm (OR: 6.2; 95%CI 2.6-15.0) were significantly more likely to go for circumcision. The transport cost incentive, 200 KES, was not significant and there was no statistical difference between the 700 and 1200 KES arms.[167]

Although the point estimates were extremely robust for the two higher incentive arms, the effect on the prevalence of male circumcision was quite low. Proportions of participants circumcised in the control, 200 KES, 700 KES, and 1200 KES arms were, respectively, 1.6%, 1.9%, 6.6%, and 9.0%. Unlike the Malawi HIV testing incentive study, the provision of small incentives did not elicit behavioral change and action in the Kenya circumcision study. This discrepancy is most likely explained by the type of health service each study examined. In the Kenyan study, adult participants were asked to go a medical procedure, circumcision, where the HIV testing study only asked participants to go back to the clinic to pick up test results. Additionally, behavioral economics reveals that individuals place greater value and emphasis on cost-benefits that are immediate versus delayed.[168] In health terms, immediate benefits would be considered treatment, where delayed benefits are preventive measures. HIV testing allows one to know their HIV status, and if positive, initiate treatment. Adult male circumcision does not have immediate benefits. The procedure is a preventive procedure to reduce one's risk of obtaining HIV and other sexually transmitted infections.[169-171]

In conclusion the effect of incentives, in both monetary form[166, 167] and as consumable goods[18, 19], while limited, is robust in enacting positive behavior change, including immunization.[18, 19] Yet, additional studies are still needed before making policy recommendations. In particular, randomized controlled trials should include incentive amounts to identify the incentive that is small enough to elicit behavior change.

In regards to the sustainability or scalability of incentives, to the knowledge of this dissertation's author, no scaled programs exist within Kenya that provide small monetary incentives for health care seeking behaviors. Although not an incentive program, the Government of Kenya's Cash Transfer for Orphans and Vulnerable Children (Kenya CT-OVC) has provided $20 USD monthly to the poorest households with orphans or chronically ill parents since 2007.[172] This suggests, that if incentives drastically improved immunization coverage levels, the Kenyan Government may support and finance their adoption.

2.7.3 **Mobile money (M-MONEY)**

While 89% of people living in high-income countries have a formal banking account, only 41% of those living in developing countries do; translating to 2.5 billion people in lower income countries without any means of saving or sending money.[173] In sub-Saharan Africa, account ownership at formal institutions is 24%, and much lower for the poorest quintile, 12%.[173] The major advantages of owning a bank account is the ability to save money to manage risks responsibly, build credit, and make transactions easier.[14, 174, 175] However, several barriers inhibit higher formal account ownership in lower income countries. In sub-Saharan Africa, 81% of individuals without an account

said they did not have enough money, it was too expensive to own an account (36%), or the branch was too far away (31%).[173]

Over 1 billion people in developing countries own a mobile phone but do not have a bank account.[176] With increasing mobile phone use, financial services are rapidly being integrated into mobile phones in what is termed mobile-money (M-Money). M-Money services include savings, insurance, credit, banking and payments, from either person-to-person, consumer-to-business, or business-to-business.[174] As of October 2012, there are 129 mobile-money networks operating in 65 lower and lower middle income countries; in 2009, there were 17 providers.[177] Many organizations have attempted to establish the current number of M-Money users.[178] Estimates include, 45 million users in 2009 with a projected 360 million by 2012[179], 100 million active users in 2011 with greater than 200 million users by 2013[180], and 133 million users in 2010 with upwards of 709 million users by 2015.[181] Irrespective of the exact estimate, mobile-money platforms are rapidly expanding.

Kenyans may prefer mobile banking to traditional banking because of the lower fees and ease of transactions. As of September 2011, over 18 million Kenyans used mobile banking services, representing 69% of all mobile subscribers and deposits totaling nearly 700 million USD in the last financial quarter.[98] M-PESA, the first and most widespread mobile money network operated by Safaricom, is a uniquely successful mobile financial services program that is widely accepted. Launched in March of 2007, there are presently 14 million registered M-PESA users, representing a 44% increase from 2010. Additionally, there are almost 28,000 M-PESA retail stores throughout

Kenya, half of them in rural locations.[182] There is ample evidence that M-PESA is penetrating to the traditionally hard to reach population.[183]

Kenya's second largest mobile phone company, Airtel, offers Airtel Money with approximately 6000 agents throughout Kenya. Essar Telecom and Telkom Orange have also launched mobile banking platforms called, respectively, yuCash and Orange Money. With the emergence of competitors, tariffs on transaction costs are likely to decrease, thereby further promoting mobile-money expansion.

The ubiquity of M-PESA in rural Kenya affords opportunity to conduct interventions and programs. One potential application of mobile-money is the use of incentives to promote positive behavior change. Where other studies have provided consumable goods or food coupons[18, 19], instead, mobile-money incentives could be provided. This alternative provides several advantages. First, the provision of mobile-money based incentives allows freedom of the recipient to spend the money as he or she sees fit, as contrasted to providing consumable goods. Second, mobile-money incentives may lessen the likelihood of theft and corruption by eliminating the need to have physical money, food coupons, or consumable goods at the health facility. Lastly, mobile-money simplifies tracking of payments through the use of a centralized account used to make transactions.

2.8 Contribution to public health

This dissertation will address gaps in the literature surrounding mobile phone ownership and texting behavior in lower income countries, identify recent estimates and predictors of immunization coverage and, often overlooked, immunization delays.

Lastly, the preliminary analysis of the M-SIMU trial, while too small and underpowered to provide solid evidence for or against the use of SMS reminders and small monetary incentives to improve immunization coverage and timeliness, will expedite the process with which results from the full M-SIMU trial can be disseminated to the scientific community and policy makers.

Although the field of mHealth is in its early infancy[15], evidence suggests that mHealth technologies are effective at promoting positive health behavior change.[16] As mHealth interventions continue to go to scale, it is imperative to study the distribution of mobile phone ownership and SMS behavior in women across different socio-demographic strata, particularly for mHealth interventions that are aimed at care-seekers. If mobile phone ownership is concentrated in older, more educated, wealthier women, mHealth interventions may not target recipients that would truly benefit from the intervention and novel routes of delivering health messages may be needed.

Few interventions available to public health practitioners and policy makers rival the cost-effectiveness of vaccines at reducing childhood morbidity and mortality.[1] Globally, the literature is plentiful concerning risk factors for being immunized[3-5] while estimates and predictors of timely immunization is just recently gaining traction in resource constrained settings.[6, 7] The identification of vaccination coverage and delay determinants is important because it allows for public health policies that implement interventions aimed at those under- and non-immunized.[8-11] Critically, the scale-up of these interventions has the potential to save millions of lives across resource-constrained countries.[12]

Despite the improvement in global immunization coverage levels, there are still countries and sub-populations that require interventions and policies that promote vaccination uptake.[21, 35] In areas where immunization coverage levels are high, the paradigm can shift from concerns about getting children vaccinated, to ensuring vaccinations are given in a timely manner. The preliminary results of the M-SIMU trial will provide some evidence as to whether demand side interventions, SMS reminders and monetary incentives, can improve immunization coverage and timeliness in a population that has relatively high immunization coverage levels, moderate vaccination delays, and adequate mobile phone ownership levels. This study is the first randomized controlled trial that employs SMS reminders for routine pediatric immunizations in lower income countries and the first to study the use of monetary incentives for immunization in sub Saharan Africa.

The evidence generated by this dissertation will assist decision makers in the Kenyan Ministry of Health, as well as those in other African countries and the greater scientific community, before committing the investment, time, and effort that will be necessary to scale-up these programs. Moreover, this project has the opportunity to demonstrate the potential of mobile phone technologies in achieving the Millennium Development Goal of reducing childhood mortality in Africa.

2.9 Tables for Chapter 2

Table 2.1 The Kenyan Division of Vaccinations and Immunizations pediatric immunizaiton schedule

Vaccine	Age at which vaccine is due				
	Birth	6 weeks	10 weeks	14 weeks	9 months
BCG	X				
Pentavalent		X	X	X	
Polio		X	X	X	
Measles					X

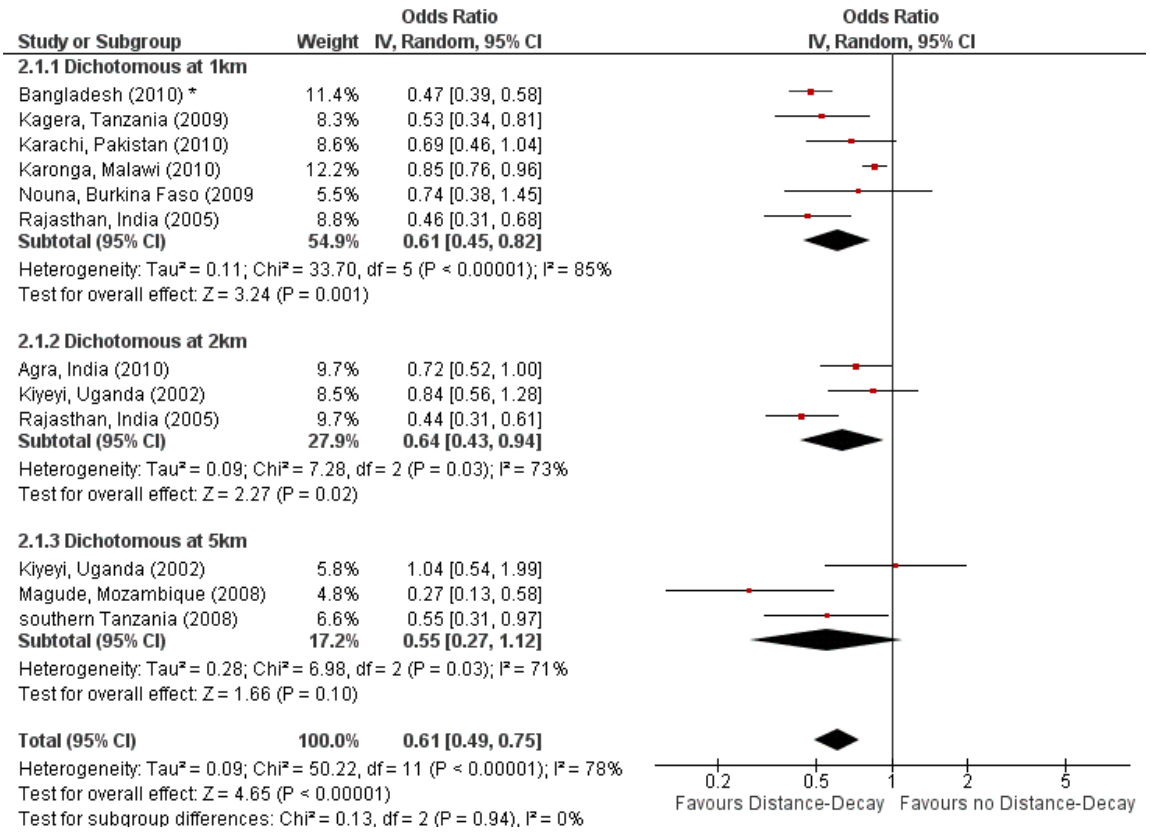
Table 2.2 Randomized Controlled Trials employing short message system (SMS) reminders to improve healthcare utilization in sub Saharan Africa

Author (year)	**Population**	**SMS reminder**	**Phone ownership**	**Result**
Lund (2014)	2550 with 1 ANC-Zanzibar	Bi-monthly + voucher	37% own Share?	13% difference in ≥4 ANC visits
Pop-Eleches (2011)	431 adults on ART-Kenya	Weekly for 48 weeks	100%- given phones	13% difference in ARV adherence
Zurovac (2011)	119 HW Kenya	2 per day for 6 months	≈100% of HW	23.7% difference in correct treatment
Odeny (2012)	1200 adults circumcised-Kenya	Daily for 1 week	100% own	5.7% difference in post-op visit
Lund (2012)	2550 with 1 ANC-Zanzibar	Bi-monthly + voucher	37% own Share?	13% difference in skilled delivery
Mbuagbaw (2012)	200 adults on ART-Cameroon	Weekly for 6 months	100%	-3.4% difference in ART adherence. NS
Lester (2010)	538 adults on ART-Kenya	Weekly for 1 year	86% own 14% share	12% diff. in ART adherence
De Tolly (2011)	2553 adults S. Africa	3 or 10 SMS Motivational or Informational	100%?	OR=1.7 Moti-10 in HIV testing

Abbreviations: ANC, antenatal care; ART, anti-retroviral therapy; HW, health worker; post-op, post-operation; NS, not significant; OR, odds ratio; SMS, short message system

2.10 Figures for Chapter 2

Figure 2.1 Pooled odds ratios and forest plot for full immunization status or 3 doses of DTP as compared to incomplete status.

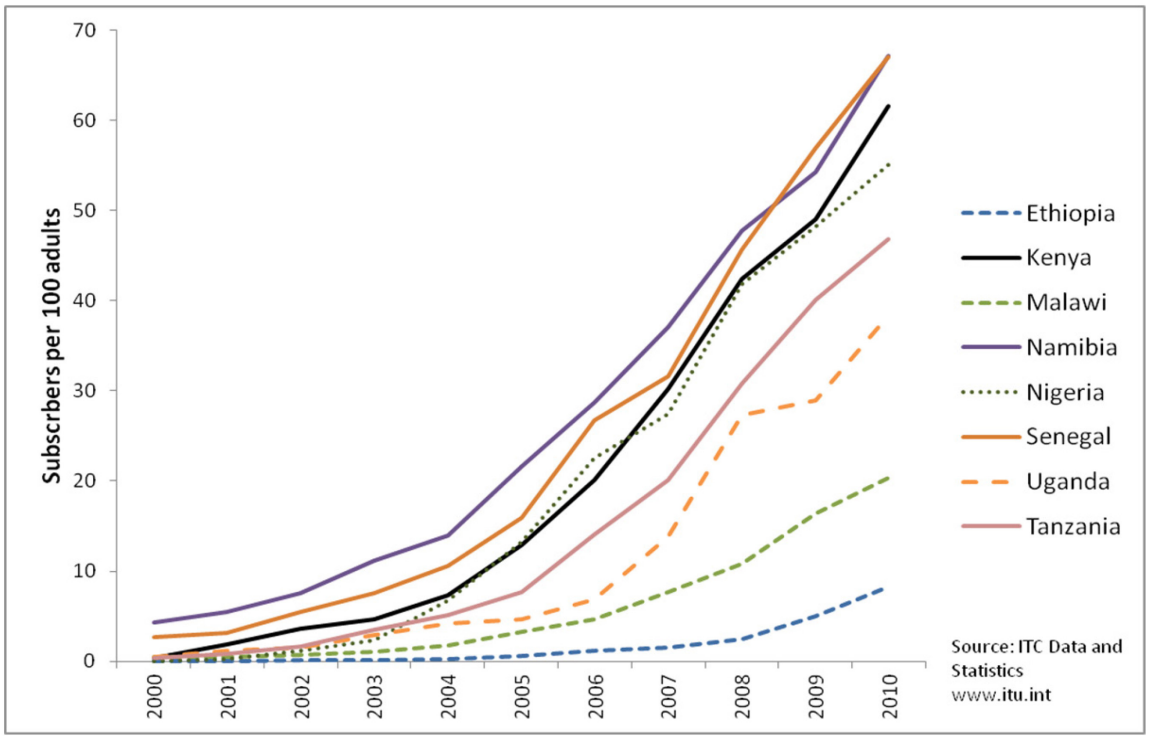


CAPTION: Reference group for each forest plot is distance closer to the health facility (i.e. <1km, <2km, <3km). This figure comes from a manuscript that is in preparation by this dissertation's author

References for studies included in forest plots:

Ghei K, et al. Arch Pediatr Adolesc Med. 2010;164(3):243-249.
Jahn A, et al. Trop Med Int Health. 2008;13(1):129-138.
Jani JV, et al. BMC Public Health. 2008;8:161.
Mohan P. Am J Public Health. 2005;95(2):241-244.
Rahman M, Obaida-Nasrin S. Salud Publica Mex. 2010;52(2):134-140.
Sanou A, et al. BMC Int Health Hum Rights. 2009;9 Suppl 1:S10.
Semali IA. East Afr J Public Health. 2009;6(1):1-5.
Tugumisirize F, et al. East Afr Med J. 2002;79(7):347-354.
Armstrong Schellenberg JR, et al. BMC Public Health. 2008;8:194.
Usman HR, et al. Trop Med Int Health. 2010;15(1):140-147.

Figure 2.2 Mobile phone subscriptions per 100 adults in eight representative sub Saharan Countries (2000-2010)



Data for this figure come from 'ITC Data and Statistics at www.itu.int

Figure 2.3 The Health Belief Model components and linkages

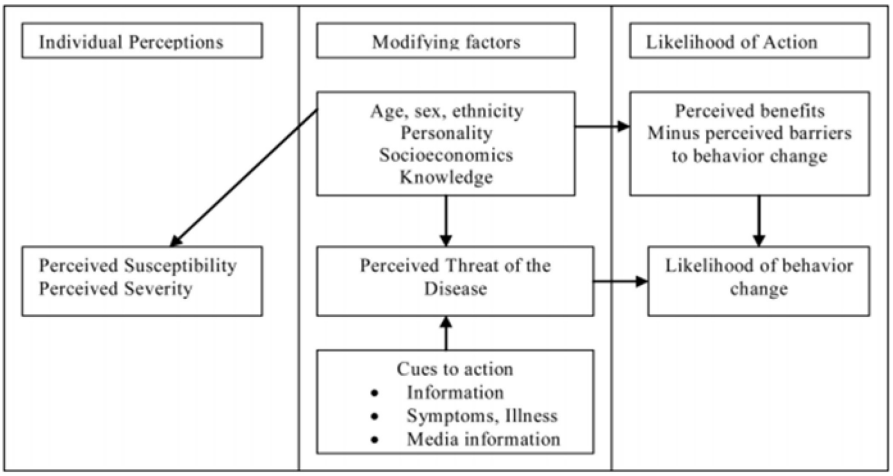
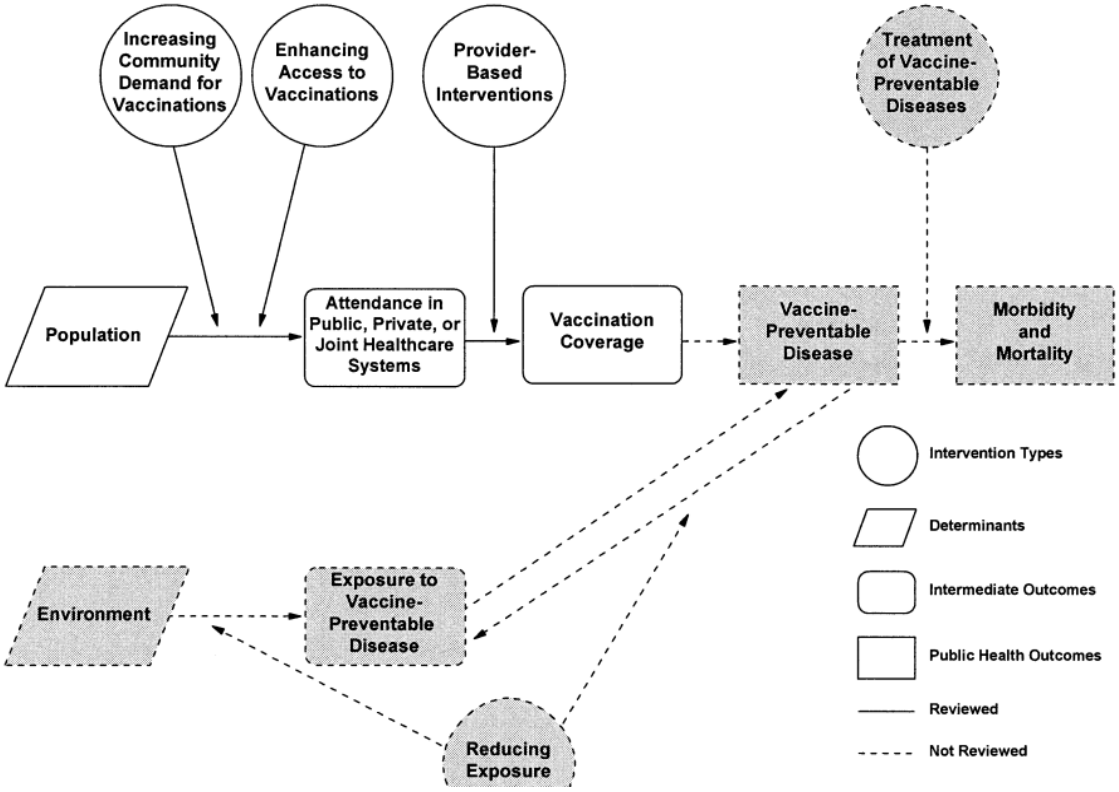


Figure 1.
Health Belief Model Components and Linkages (Hochbaum, 1956, Rosenstock, 1966, Becker, 1974 & 1977)

Image from Rahman International Journal of Cancer Prevention. 2008 January 1; 2(6): 415–425

Figure 2.4 Intervention points for increasing immunizaiton coverage



Briss, P et al. Reviews of Evidence Regarding Interventions to Improve Vaccination Coverage in Children, Adolescents, and Adults. American Journal of Preventive Medicine. 2000;18(1S)

Figure 2.5 Distribution of vaccination timelines for pentavalent1 and pentavalent2 vaccines from the M-SIMU feasibility study conducted in Siaya, County Kenya (2011)

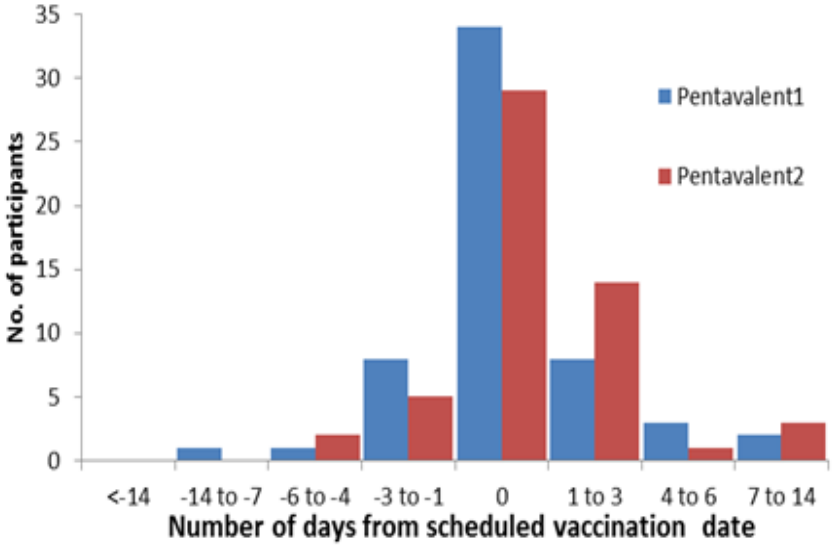


Image adapted from Wakadha, H., Chandir, S., Were, E., Rubin, A., Obor, D., Levine, O., Gibson, DG., Odhiambo, F., Laserson, K., Feikin D. The feasibility of using mobile-phone based SMS reminders and conditional cash transfers to improve timely immunization in rural Kenya. *Vaccine.* 2013 Jan 30;31(6):987-93

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Chapter 3. Methods

3.1 Introduction

The dissertation's primary aims all arise from various components of the Mobile Solutions for Immunization (M-SIMU) village randomized controlled trial. An overview of major project milestones is found in Figure 3.1. Prior to M-SIMU enrollment, an immunization and mobile phone ownership survey was conducted to inform sample size and randomization requirements of the randomized trial. Moreover, focus group discussions were conducted to assist with the construction of SMS reminders, incentive amounts, and to help foresee any potential problems with mobile-health (mHealth) interventions. The baseline survey provides data for primary aims #1 and #2. The focus group discussion findings are included in primary aim# 2. Primary aim #3 utilizes pilot data from the M-SIMU trial. *A priori*, the first 107 infants who were enrolled and had 12 month follow-up completed were excluded from the larger trial's formal analyses. This cohort was created to assess the readiness of the automated SMS system to correctly deliver SMS reminders This preliminary cohort received all study procedures as those in the formal randomized controlled trial and serve as the data source for primary aim#3.

A brief overview of the study setting will start this chapter followed by a detailed description of the M-SIMU study design, randomization procedures, study objectives, and sample size requirements; all conducted by this dissertation's author. Next, data collection, independent and dependent variables, and statistical analyses will be described for each primary aim and followed up a discussion of ethical issues.

3.2 Study setting

This dissertation's studies were conducted in villages within the Kenyan Medical Research Institute and Centers for Disease and Control (KEMRI/CDC) Health and Demographic Surveillance System (HDSS). The HDSS is located within Siaya County, Nyanza Province in western Kenya and includes Asembo and Gem Districts (Figure 3.2). Since 2001, the HDSS has systematically collected vital events; including births, deaths, and pregnancies for a population of over 220,000 individuals.[1] In addition, every fourth months HDSS staff conduct household visits to collect disease morbidity estimates and socio-demographic indicators. The HDSS has served as a platform for numerous scientific studies, including randomized controlled trials for bed-net efficacy, and rotavirus vaccine efficacy.[2, 3]

Nyanza Province is one of Kenya's poorest provinces.[4] The major health indicators, such as infant mortality rate and third dose coverage of DTP are worse than national averages (Table 3.1). The predominant occupation of Gem and Asembo habitants is subsistence farming and the majority of people belong to the Luo ethnic group. Compounds, consisting of 2 to 6 households, are widely dispersed across a bushy landscape that is pockmarked with small farming fields. The north and south are bound by paved roads, with only dirt roads cutting through central Gem District.

Malaria transmission continues to be holoendemic and occurs year-round.[5, 6] The HIV prevalence among women aged > 13 years old was 15% in 2010, as determined by a home-based counseling and testing program (K. Laserson, KEMRI/CDC personal communication). The area has a high under-5 mortality rate (U5MR), 212 deaths per 1,000 live births, with pneumonia and diarrhea as common causes of childhood

mortality.[6] In Gem, unpublished DSS data found that coverage with the third dose of pentavalent vaccine was 38% at 18 weeks of age and 54% by 24 weeks of age in 2010. By ages 12-23 months, the pentavalent3 coverage had increased to 83%, suggesting both the need for efforts at increasing vaccine coverage and vaccine timeliness.

From 2003-2010, Gem was part of a Health and Demographic Surveillance System (HDSS) run by KEMRI/CDC.[5] In August 2010, the full HDSS stopped in Gem due to lack of continued funding. KEMRI/CDC has maintained good relationships with the community throughout this period and has gained the trust and collaboration of the leaders and citizens of central Gem. Pregnancy, births, and deaths were still collected from Gem District while the HDSS was postponed.

The study area has approximately 24 health facilities where immunizations are given. The majority of these health facilities are government operated and staffed by the Kenyan Ministry of Health. The supply of vaccines to areas clinics is maintained by a push system with tri-monthly delivery of vaccines from the District Ministry of Health (DMOH). If clinics run out of vaccines between these tri-monthly deliveries, they can request more vaccine from the DMOH. Periodic vaccine stock-outs, most often measles and/or BCG, do occur in Gem clinics and are often due to lack of transportation to get the vaccines to the clinic or poor planning to predict impending deficits. There are little problems with pentavalent supply at each clinic, unless there is a national stock-out which will affect clinics country wide.

3.3 The Mobile Solutions for Immunization trial (M-SIMU)

As discussed previously, the sample for the third manuscript (Chapter 6) comes from the first 107 infants that completed 12 month follow up visits. All study procedures

in this preliminary cohort were conducted in the same manner as those infants in the parent trial. A more detailed description of M-SIMU study procedures, as compared to methods from Chapter 6, follows.

3.3.1 **Study design**

The M-SIMU study was a four-arm cluster randomized controlled trial. Villages, as defined by the KEMRI/CDC Health and Demographic Surveillance System (HDSS), were the units of randomization. Villages were randomized to one of four study arms in a 1:1:1:1 allocation ratio in September, 2013 (Figure 3.3). The study arms included: (1) Control; (2) SMS reminders; (3) SMS reminders plus 75 Kenyan Schillings (KSH; 85 KSH=1USD); and (4) SMS reminders plus 200KSH. SMS reminders were sent both three days and one day before immunization doses scheduled at 6 weeks, 10 weeks, 14, weeks, and 9 months. Incentives were delivered to the participant's mobile phone if the participant's child is brought for immunization within two weeks of the scheduled date. All eligible mothers/caretakers residing within a study village were assigned to the study arm that the village was allocated.

3.3.2 **Randomization**

The GAUSS™ Mathematical and Statistical System (Aptech Inc., Chandler, AZ) was used to conduct a constrained randomization. The GAUSS program iterated until 5000 acceptable randomizations were found that met the following criteria:

> +/- relative 10% over all 152 villages for the means of the variables: full immunization coverage, phone ownership, distance to the nearest clinic, and village population of children 12-23 months old .

+/- relative 25% within each region (Asembo, Gem) for the means of the variables: full immunization coverage and phone ownership.

The randomization was also stratified on region such that each study arm contained 30 villages from Gem and 8 villages from Asembo region. Data for the randomization came from a baseline survey conducted within the study area in March-April 2013.

3.3.3 **Setting and participants**

Villages were included in the study if they resided within either Gem or Asembo HDSS boundaries. Villages were excluded from the M-SIMU study if there were active immunization intervention/programs (e.g. NGO outreach immunization clinics) that would interfere with the study objectives. Sample size calculations were conducted to determine the number of villages needed to be able to detect a 15% absolute difference in full immunization coverage at 12 months of age between control and intervention arm.

To ensure accurate population numbers, KEMRI/CDC HDSS casually employs 'village reporters' to identify births, deaths, and pregnancies within their community. For the M-SIMU trial, village reporters identified new births and sent a birth notification SMS to the RapidSMS server, a free and open-source platform (Figure 3.4). The notification SMS included the study village and compound number. The RapidSMS server automatically relayed the notification to a Community Interviewer (CI). The CI visited newborn's compound to explain the trial and screen the mother/caretaker for the following eligibility criteria:

Inclusion Criteria:

1) Mother of infant aged 0-4 weeks during the study period

2) Current resident of one of the study villages

3) Willing to sign informed consent for the study

Exclusion Criteria:

1) Plans to move out of the study area in the next 6 months

2) Has already received immunizations other than birth dose of BCG or polio

Mothers were eligible independent of mobile phone ownership. Mothers only needed to have access to a mobile phone, whereby access was defined by the mother and could include someone that lives in household, compound or a neighbor. If no phone was identified, community interviewers were tasked to deliver incentives. According to our baseline survey, 94% of mothers owned or had access to a mobile phone within the compound (See Chapter 5).

Eligible mothers were required to provide both oral and written informed consent to the Community Interviewer. Upon providing consent, the Community Interviewer sent an enrollment SMS to the RapidSMS server that contained the mother's village and compound number, the phone number that can be used to receive an SMS, the child's date of birth, the preferred language to receive SMS's (English, Kiswahili, or Dholuo), and the baby's first and last name. Upon completion of a successful enrollment SMS, the RapidSMS server sent a personalized SMS to the mother (Table 3.2).

3.3.4 **Control and intervention arm descriptions**

The interventions, SMS reminders and incentives, were designed to motivate mothers and increase demand for routine pediatric immunizations.

SMS reminders

SMS reminders were a component of all three intervention arms. SMS reminders were sent using RapidSMS on both 3 days and 1 day before the scheduled immunization visits at 6,10, and 14 weeks for the three doses of pentavalent vaccine and at 9 months for measles as per Kenyan Expanded Programme on Immunization (KEPI) guidelines. SMS reminders were sent as text messages in English, Kiswahili or Dholuo language, according to the mother's preference as indicated at enrollment. If a pentavalent vaccination was given later than the scheduled date, then the SMS reminders for the subsequent pentavalent dose were reprogrammed to occur at four weeks from the date of vaccine receipt, as per KEPI guidelines.[7] As an example, if a child received pentavalent1 at 8 weeks of age (scheduled to be given at 6 weeks), the immunization reminders for pentavalent2 were sent when the child was 12 weeks old (instead of the KEPI schedule of 10 weeks).

SMS reminders were composed of a core text and a motivational saying (Table 3.2). The core message stated which vaccine is due this week. If the participant was in an incentive arm, the SMS also contained the amount of money the mother would be remunerated for timely vaccinating her infant. The motivational sayings attached at the end of the SMS were chosen from the results of a Focus Group Discussion on using mobile phones to improve immunizations (See Chapter 5). The four sayings included in M-SIMU SMSs were: "Vaccines save Kenyan babies lives", "Baby < INSERT BABY FIRST NAME> is happy when healthy "Most <INSERT DISTRICT: ASEMBO or GEM> babies get vaccinated, be one of them", and "Vaccines are available now". For each vaccine dose, one of the four motivational sayings was randomly selected, with

replacement, by the RapidSMS software. The same motivational saying was used for the 3 day and 1 day reminder for that particular vaccine dose.

Incentives

Mobile phone based monetary incentives were a component of study arms #3 and #4. The delivery of the incentive in arms #3 and #4 was identical; only the incentive amount differed. In addition to SMS reminders, mothers were sent either 75KSH or 200KSH (arm #4) to the mobile phone number they identified at enrollment for each timely dose of pentavalent and measles vaccine, defined as within 2 weeks of the scheduled date (i.e., pentavalent1 at 6 weeks, pentavalent2 and pentavalent3 four weeks after the previous dose and measles at 9 months.) If a mother brought her child for vaccination after 2 weeks of scheduled date, no incentive was transferred. Cash transfers were done using the preferred mobile money network of the participant and were to be delivered within 24 hours of vaccine receipt.

The incentive amounts in arms #3 and #4 were guided by opinions of mothers, village reporters, and local transport costs. The intent of the incentive was to help offset the costs associated with transportation to the clinic. The transaction costs associated with mobile-money transactions were borne by the study such that mothers will receive the full amount indicated.

Control

Mothers that resided in control arm villages received a congratulatory SMS at enrollment which included a general-health related saying, “The greatest wealth is health”. No additional SMS’s or incentives were sent to mothers. At the 12 month

follow-up visit, community interviewers referred mothers of under-vaccinated children to the nearest clinic.

3.3.5 **Study objectives**

The following primary and secondary objectives are for the formal M-SIMU trial and do not necessarily represent objectives of this dissertation.

Primary objective

The study was powered to determine if SMS reminders, with or without incentives, could increase the percentage of fully immunized children (FIC) by 15% as compared to control group at 12 months of age in rural western Kenya. A fully immunized child was defined as children that received one dose of BCG, 3 doses of pentavalent and polio, and 1 dose of measles vaccine.

Secondary objective

The study assessed several secondary objectives that primarily focused on timely receipt of individual vaccines and effect modifiers on the primary outcome. These secondary objectives included:

1. To determine if interventions increased timely vaccine coverage by 15% as compared to control group at 10 months of age

2. To determine if interventions increased the percentage of children vaccinated within 2 weeks of each scheduled vaccine date compared with control group;

3. To determine if interventions decreased drop-out in vaccination between first and third pentavalent dose compared with control group;

4. To determine if the 200KES arm increased timely vaccine coverage, increased the percentage of infants vaccinated within 2 weeks of scheduled date, and decreased drop-out between 1st and 3rd dose of pentavalent vaccines as compared to the 75KES arm;

5. To determine if either the 75 or 200 KES arm increased timely vaccine coverage, increased the percentage of infants vaccinated within 2 weeks of scheduled date, and decreased drop-out between 1st and 3rd dose of pentavalent vaccines as compared to the SMS alone arm;

6. To determine if measles vaccine coverage varied by study arm;

7. To determine if pentavalent3 vaccine coverage varied by study arm;

8. To determine if there was a differential effect on vaccine coverage based on owning one's own phone versus using someone else's phone;

9. To determine if there was a differential effect on vaccine coverage based on residential distance from a health facility;

10. To determine if the interventions impacted other indicators of health status, including anthropometric measurements (e.g. weight-for-height, weight-for-age), bed-net usage, vitamin A coverage, retention of the "maternal child health" card, and all-cause mortality;

11. To evaluate the direct costs for each intervention arm per additional child vaccinated beyond the status quo (i.e. control group);

3.4 Data collection

3.4.1 Primary Aim #1

The first primary aim was to determine immunization coverage and timeliness using data from a baseline survey of the M-SIMU trial conducted in March and April of

2013. This survey is also the source of data for primary aim #2 (excluding the focus group discussion portion). The questions for this survey were selected from a cache of HDSS surveys that are routinely used for immunization coverage. Specifically, questions for our baseline survey came from the KEMRI/CDC HDSS Bed-net form, Religion, Ethnicity, and Marriage form, Education Status Form, Immunization Form, and Household Socio-Economic Form. A written version of the pooled questions was provided to a KEMRI/CDC programmer to digitize the survey (Appendix 1). The surveys were constructed using ODK collect and placed on Huawei Y200 simple smart phones. Skip patterns and quality checks were programmed into ODK to help minimize potential errors in data entry and analysis. The survey was piloted by KEMRI/CDC staff members and revisions to survey were made as needed.

Prior to commencement of baseline survey, twenty-two KEMRI/CDC Community Interviewers underwent five days of training. Each survey question was discussed in Swahili, Luo, and English language. One day was spent doing role-play interviews in front of the trainees. The last day, community interviewers piloted the baseline survey in the field. Additionally, community interviewers were taught research ethics, interview techniques and handling methods of the mobile phone. Of note, the majority of the community interviewers were previously employees of KEMRI/CDC or had experience administering surveys with other local organizations

With a census of HDSS consented households, community interviewers approached eligible households and asked the compound head if they could interview the caregiver of the child between the ages of one and two years. Staff members then asked the caregiver if the maternal and child health (MCH) booklet was available, and if so,

immunization dates were entered into the mobile-phone based survey. If no MCH booklet was present, staff collected immunization history through verbal report. Verbal report of BCG vaccination was validated by examination of infant's arm for a scar. No efforts were made to validate other vaccinations. Data was cleaned continuously after data entry and missing or questionable data points were relayed back to field staff for follow-up visits.

3.4.2 **Primary Aim#2**

The second primary aim is to assess the mHealth preparedness of the community through focus group discussions and a baseline survey of mobile phone ownership and text messaging behavior. As the data source for mobile phone ownership and SMS behavior was the same survey used in primary aim #1, this section will focus on focus group discussion.

A semi-structured questionnaire guide was used to elicit mother's responses on barriers to immunization, SMS reminders for pediatric immunization dates, and monetary incentives to motivate mothers to bring children for immunization (Appendices 2 and 3). This guide was created by members of the Johns Hopkins study team and edited by KEMRI/CDC staff to ensure cultural appropriateness. The focus group discussion was piloted twice with community interviewers playing the role of participants.

A total of thirty women participated in one of three focus group discussions over the span of two days in June 2013. Prior to the group discussions, participants were individually surveyed by KEMRI/CDC study staff to assess mobile phone literacy. Focus group discussions, lasting approximately 2-2.5 hours were audio recorded, transcribed

into Dholuo, and then translated into English. Audio recordings were destroyed after transcription and translation. Mothers were given participant IDs, which were used to identify women during the focus group discussions. No names were recorded during discussions or written on questionnaires.

During the focus group discussion, we required individual responses of participants. For these questions, participants either wrote the answer on a small piece of paper or placed a pre-printed response in bins labeled #1 (i.e. favorite, preferred, best), #2 (i.e. second favorite, preferred, best), etc. De-identified responses from individual surveys and group discussions were entered into Microsoft Excel and stored on the secure KEMRI/CDC network.

3.4.3 **Primary Aim#3**

Primary aim #3 is to determine the effect of SMS reminders with or without monetary incentives on timely immunization of pentavalent3 and measles vaccines. *A priori*, the first 107 M-SIMU participants that completed a 12 month follow-up visit were designated as a pilot cohort to assess the performance of SMS delivery system and survey instruments. These participants underwent all study procedures as those in the formal (non-pilot) trial and serve as the population for this dissertations third primary aim.

The M-SIMU study is designed to minimally interfere with routine care-seeking behaviors of mothers and routine delivery of care by health practitioners. Participants were interviewed, at most, six times. All participants were interviewed at enrollment when infant was between 0 and 4 weeks old and at follow up when the infant was 12 months old. If a mother brought her infant for vaccination at an M-SIMU clinic, there

was a short interview for each of the four immunization visits (pentavalent1, pentavalent2, pentavalent3, and measles vaccines).

Eight community interviewers from the baseline survey in primary aims #1 and #2 were rehired for the randomized controlled trial to conduct screening, informed consent, enrollment surveys, and follow-up surveys. Community interviewers underwent five days of training in August 2013 where refresher courses on interview techniques and research ethics were provided. The screening, consent form, and enrollment survey were also presented to the Community Interviewers and each section was discussed in Swahili, Luo, and English languages. Informed consent and enrollment role plays occurred during the training session and community interviewers piloted the instruments in the field. The screening form and enrollment survey were conducted using ODK Collect software installed on a simple smart mobile phone (Huawei Ascend Y200 model). Information collected at enrollment includes mobile phone literacy, demographics, vaccine perceptions, transportation, and socioeconomic status. After the enrollment survey was completed, community interviewers sent an enrollment SMS to the KEMRI/CDC based RapidSMS server (Figure 3.4).[8] This SMS included the infant's village number, compound number, first and last names, preferred language to receive SMS, and the caregiver's mobile phone number.

To prospectively document immunization status, KEMRI/CDC health facility recorders were stationed in twenty-four health facilities that resided within the study setting. Health facility recorders were rehired from the M-SIMU baseline survey or from other KEMRI/CDC projects and underwent training similar to the community interviewers.

All infants that presented to M-SIMU health facilities were queried by Health Facility recorders for their M-SIMU enrollment status. Enrollment status was confirmed using enrollment lists located on password protected netbooks. For enrolled children, the health facility recorder sent an SMS message to the RapidSMS server after an enrolled infant was vaccinated (Figure 3.4). This SMS contained the child's study id, the date of vaccination, which vaccine was received, and the new phone number if the mother has changed phone lines. After the vaccine receipt SMS was sent, health facility recorders interviewed participants using a net-book based questionnaire.

For clinics where few immunizations are given per day, there was no permanent health facility recorder stationed due to financial constraints. Rather, health facility recorders from neighboring clinics visited these smaller clinics at the end of the day, collected immunization information for enrolled mother-infant pairs, and sent the vaccine receipt SMS to RapidSMS system.

When enrolled infants reached 12 months of age, community interviewers conducted in-home follow up visits to ascertain immunization status and collect information on mothers' perceptions of intervention. Surveys were conducted using the ODK application loaded on a simple smart phone as described during the enrollment procedures. Community Interviewers also hand-wrote immunization dates on a paper form as a measure of double-data entry.

3.5 Definition of dependent variables

3.5.1 Primary Aim #1

Data for primary aim#1, to estimate prevalence and risk factors for delayed vaccination and not receiving immunization were collected from a baseline survey of the

M-SIMU trial. The two primary outcomes were infants that did not receive vaccination and infants with delayed vaccination. Analyses for infants that did not receive vaccine were restricted to pentavalent3, measles vaccine, and fully immunized coverage (FIC), defined as infants that received BCG, three doses of pentavalent vaccine, three doses of polio vaccine, and measles vaccine. Analyses for infants that received delayed vaccination were restricted to pentavalent1, pentavalent3, measles vaccine, and FIC. The proportion of infants not receiving a vaccine was generated for each vaccine and defined as:

$$\%\ not\ vaccinated = \frac{n\ infants\ not\ vaccinated}{N}$$

where, N= the full sample of infants

For each regression model, non-vaccination was defined as dichotomous variable with infants that did not receive vaccination coded as a 1 and infants that received vaccination as 0.

An infant was labeled delayed if vaccination occurred greater than four weeks from the Kenyan Division of Vaccination and Immunization (DVI) scheduled date.[9] For pentavalent1, pentavalent3, and measles, infants were labeled delayed if vaccinated after 10 weeks, 18 weeks, and 302 days, respectively. Delayed FIC was defined as infants that received at least one vaccine after 12 months of age, given that all eight vaccines were received. The proportion of infants with delay for a vaccine was generated for each vaccine and defined as:

$$\%\ delay = \frac{n\ infants\ delayed\ vaccine}{n\ infants\ that\ received\ vaccine}$$

For each regression model, delayed immunization was defined as a dichotomous variable with infants that were vaccinated with delay coded as 1 and infants that were timely vaccinated coded as 0.

Underimmunization was defined as an infant that neither received the vaccine nor received the vaccine within four weeks of the scheduled date. Severely underimmunized infants were defined as the proportion of infants that were underimmunized for greater than 90 days in the first 12 months of life and were delayed for three of five vaccines (BCG, pentavalent1, pentavalent2, pentavalent3, and measles). Infants were not severely underimmunized if the total number of days underimmunized was less than 90 days or if less than three vaccines were received with delay.

$$\%\ severely\ underimmunized = \frac{n\ infants\ severely\ underimmunized}{N}$$

where, N= the full sample of infants

For each regression model, severely underimmunized was defined as dichotomous variable with infants that were severely underimmunized coded as a 1 and infants that were not severely underimmunized coded as 0.

3.5.2 **Primary Aim #2**

Data for primary aim#2, to estimate mobile phone ownership levels, SMS utilization, and their respective predictor variables were collected from a baseline survey of the M-SIMU trial. All three primary outcomes were self-reported by caregivers with infants aged 12-23 months and analyzed using logistic regression. Mobile phone ownership was coded as '1' if the mother owned a mobile phone and coded as '0' if the mother either shared or did not own a mobile phone. For receiving and sending SMS primary outcomes, participants were asked if they received or sent an SMS in the past

week. Participants that replied yes were coded as '1' and participants that replied no were coded as '0'.

3.5.3 **Primary Aim #3**

Data for primary aim#3, to determine the effect of SMS reminders, with or without monetary incentives, on pentavalent3 and measles vaccination, arose from the first 107 participants with completed M-SIMU 12 month follow-up visits. The two primary outcomes were pentavalent3 vaccination and measles vaccination. To determine a final immunization status for pentavalent and measles, decision trees were generated and employed based on whether the mother provided a maternal and child health card (MCH) (Figure 3.5) or oral report (Figure 3.6). A child was defined as vaccinated for measles or pentavalent3 if there was written confirmation independent of the M-SIMU study staff's records (i.e. the immunization SMS sent by the health facility recorder). Infants with maternal and child health booklet at follow-up was sufficient for determining primary outcomes, unless there was discrepancy with dates from immunization SMS records, in which case, the clinic immunization log book was used to resolve date differences. For those that orally reported at follow-up, clinic records were searched and immunization date recorded.

The infant's age at vaccination was calculated by subtracting the infant's date of birth from the date of vaccination. Infants were considered vaccinated with pentavalent3 by 24 weeks of age if the infant received the three dose pentavalent sequence before the infant aged to 168 days (24 weeks). Infants were considered vaccinated with measles vaccine by 10 months of age if the infant received measles vaccine by 302 days of age

(10 months). The measles primary outcome was independent of child's pentavalent3 status.

3.6 Statistical analyses

3.6.1 Primary Aim #1

Data were explored for incomplete or nonsensical immunization data (i.e. pentavalent vaccine given before child was born). Crude risk ratios with 95% confidence intervals were obtained by binomial regressions with log link function were conducted to obtain crude risk ratios and their 95% confidence intervals for each of the independent variables.

$$Log((P(Y=1)/(Pr(Y=0)) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + ...\beta_n X_n$$

where Y = immunization outcome, Y=1 for participants that were delayed, did not receive immunization, or were severely underimmunized and Y=0 for participants that were timely immunized, received immunization, or were not severely underimmunized.

Three separate models were used for the three primary outcomes. The first model compared infants who did not receive vaccination to infants who received vaccination. The second model compared infants that received vaccinations with delay to infants that received vaccinations on time. The third model compared infants that were severely underimmunized to infants that were not severely underimmunized. Variables that were included in final adjusted models were selected using forward-stepwise selection with an alpha of 0.05. Analyses were performed using STATA/IC, version 11.2 (Stata Corp, College Station, Texas). An alpha of 0.05 was used for all hypothesis testing.

3.6.2 **Primary Aim #2**

Prior to construction of regression models, data were checked for completeness and accuracy. Three separate models were used to obtain odds of mobile phone ownership as compared to odds of not owning a mobile phone; odds of sending an SMS in the past week as compared to odds of not sending an SMS in the past week; and odds of receiving an SMS in the past week as compared to odds of not receiving an SMS in the past week. Unadjusted odds ratios with 95% confidence intervals were obtained using bivariate logistic regressions for each of the independent variables.

$$Log((P(Y=1)/(1-Pr(Y=0)) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + ...\beta_n X_n$$

where Y = dichotomous mobile phone ownership with 1= a mother that owned a mobile phone and 0= a mother that did not own a mobile phone; Xn = covariates

Variables for final multivariate models were selected using forward step wise Akaike Information Criteria.[10] Potential interactions were explored and included in model if statistically significant. Additional models for odds of receiving and sending SMS with the mobile phone ownership variable were also created. An alpha of 0.05 was used for all hypothesis testing.

3.6.3 **Primary Aim #3**

Cluster level and individual level estimates of baseline variables were generated for each study arm and visually inspected to see if there were any differences in study arms. The large number of clusters per study arm allowed us to conduct individual level analyses as compared to cluster level analyses. Individual analyses were favored because of their efficiency and their ease to adjust for covariates in a single.[11]

Analyses were first conducted using intention-to-treat (ITT) for delivery of SMS reminders. Per protocol analyses were conducted to support ITT analyses.[12] Inverse Kaplan-Meier curves were created for the pentavalent3 and measles primary outcomes.[13-15] Infants were censored at 24 weeks for pentavalent3 and 302 days for measles if the vaccine was not received by the respective time points. As applicable, infants were censored at age of death or out-migration if vaccine was not received. Log rank tests with trend option were used to assess the global equality of inverse survival curves and differences in trends across the four study arms.[16] To assess the proportional hazards assumption for Kaplan-Meier survival analysis, log-log plots were created and visually assessed for parallel curves.[17] Additionally, the proportional hazard assumption for Cox regression models was tested based on examination of Schoenfeld residuals.[18]

Cox regressions that included adjustment for the cluster design of the trial by use of robust variance estimates of immunization status at village level[19] were employed to obtain unadjusted hazard ratios and 95% confidence intervals by study arms for pentavalent3 and measles vaccination.[20]

$$Log((H(t)/(H_0(t)) = i.\beta_1 StudyArm$$

Where H(t) is equal to hazard at time t for measles or pentavalent3 vaccination and H0(t) is equal to baseline hazard at time t for those with all predictor variables equal to 0

For all models, study arm was entered into the model as a dummy variable where the control arm served as the reference group. *A priori*, we included mobile phone ownership, region, and time to clinic in multivariate Cox regression models.

$$Log((H(t)/(H_0(t)) = i.\beta_1 StudyArm\ \beta_1 MobilePhone + \beta_2 Region + \beta_3 Time$$

Additional variables were included in adjusted Cox regressions if there were differences in their distribution by study arm and if their unadjusted Cox regression estimates were statistically significant. Added variables to multivariate models were included with the 'strata' option to allow for different baseline hazards of covariates. Effect modifications of mobile phone ownership and time to clinic on pentavalent3 and measles vaccinations by study arm were explored. An alpha of 0.05 was used for all hypothesis testing. Analyses were performed using STATA/IC, version 11.2 (Stata Corp, College Station, Texas).

3.6.4 **Power calculations for M-SIMU**

The sample size for the M-SIMU preliminary cohort was predetermined. With a fixed sample size, control arm survival probabilities (that is the proportion of those not vaccinated) surrounding the observed survival probabilities of pentavalent3 and measles vaccination were varied to assess the power of different effect estimates (Figure 3.7).

Power calculations were calculated for comparisons of 200KSH arm (n=27 infants) to control arm participants (n=22 infants). Survival probabilities of control arm participants at 16 weeks for pentavalent3 (60%) and 286 days for measles vaccination (50%) were used to generate survival probabilities for hazards ratios ranging from 1.5 to 3.0. The control arm survival probabilities were varied +/- 10 absolute percentage points. For pentavalent3 and measles vaccination, we had approximately 50% power to detect a hazard ratio of at least 2.0 for the primary vaccination outcomes

3.7 Ethical considerations

The study protocol received ethical clearance from the Scientific Steering Committee (SSC), the KEMRI-Nairobi Ethical Review Committee (ERC; SSC#2409), Johns Hopkins University Bloomberg School of Public Health (deferred ethical clearance to KEMRI); Centers for Disease Control and Prevention (deferred ethical clearance to KEMRI) (Appendices 4 and 5). Letters of support were obtained from the Provincial Ministry of Health and District Ministries of Health. Extensive community mobilization activities occurred prior to the start of the trial. These activities entailed meetings with village elders, chiefs, and Community Advisory Board members. A large focus of these activities was explaining to the community that different villages will be receiving different interventions (i.e. you may not receive an incentive) and that no experimental vaccines will be given. The trial is registered with ClinicalTrials.gov as NCT01878435.

Data storage and study participant confidentiality:

Interviews and surveys were conducted privately and participants were told that their participation was voluntary. Data and study forms were kept confidential. Data were stored in a secure database, either in a locked file cabinet or password -protected computer, at the study headquarters in KEMRI/CDC-Kisian. This field site has 24 hour security and requires identification badges and key-codes for entrance. A limited number of authorized staff was allowed access to the data. Staff that had access to data were required to sign a document stating they agree to maintain confidentiality of participants' personal records.

For focus group discussions, mothers were given ID numbers which were used to identify women throughout the focus groups. No names were recorded during

discussions or written on questionnaires. Audio recordings of focus group discussions were destroyed after transcription and translation to English language.

Consent process

For focus group discussions and the M-SIMU trial, community interviewers approached eligible mothers and explained study procedures, risks involved, any potential benefits, participation was completely voluntary, and participants could withdraw from study at any time. Community interviewers allowed ample time for any questions from potential participants. The informed consents were provided in English, Dholuo, and Kiswahili languages (Appendices 6 and 7). In rare instances where a mother or caretaker was illiterate, verbal consent was sought in the presence of someone who was neither study staff nor a family member. For the M-SIMU trial, if participants were interested in participation, a short screening form was administered

Risks

For the M-SIMU randomized controlled trial and focus group discussions, the risks assumed by study participation were minimal. M-SIMU specific risks included:

1. Potential inconvenience from survey questions. Some people might find the questions asked of them take too much time out of their day.
2. Potential anxiety or discomfort from not being randomized to an incentive arm.
3. Potential invasion or loss of privacy

There was no physical risk to the mother or infant as a result of their participation. All vaccines given in the study were routine immunizations recommended by the Kenyan MOH EPI program. Although there were risks of adverse events associated with

vaccines, the trial does not require infant vaccination for participation. No experimental or unapproved vaccines were given. Furthermore, no biological samples were taken.

Minimizing risks

The risks associated with inconvenience of time were minimized by ensuring that the field staff was well trained in survey administration and reminding mothers that their participation was completely voluntary. There were several short surveys conducted at several time points. These included enrollment and screening surveys conducted at participant's house, a twelve month follow-up survey conducted at participant's house when infant aged 12 months, and up to four surveys conducted at clinic, if infant was vaccinated. No sensitive questions, such as HIV status were asked throughout the trial.

Risks of anxiety or discomfort felt by participants that were randomized to a non-incentive arm were minimized by the study's decision to conduct a public randomization ceremony. Village chiefs and community members were involved with randomization and allocation of study arms. Intensive community mobilization efforts were made prior to study initiation.

Risks of invasion or loss of privacy were minimized by conducting surveys in private areas at the both the household and immunization clinic. Additionally, study records were de-identified, kept in locked cabinets and/or password protected computers, and their access was restricted to principal investigators and those involved with data collection and analysis.

Potential benefits to participants

Possible benefits to the child included improved timeliness of immunizations. Some mothers received incentives up to 800 Ksh ($10 USD) if their infant was brought on time for pentavalent1, pentavalent2, pentavalent3, and measles vaccine, an amount she would typically not have received if not for this trial. The results of this study will be shared with the Kenyan Ministry of Health and may help future Kenyan infants in receiving more timely immunizations.

3.8 Tables for Chapter 3

Table 3.1 Socio-demographic indicators for Gem District, Nyanza Province, and Kenya

Indicator	Gem, Kenya (HDSS 2008)	Nyanza Province, Kenya (KDHS 2009)	Kenya (KDHS 2009)
Mid-year population	83,059 thousand	5.4 million	39.4 million
% population < 5 years old	17.2%	*NA*	15.7%
Crude Birth Rate	39.8	*NA*	34.8
Total Fertility Rate	5.7	5.4	4.6
Neonatal Mortality Ratio (deaths per 1000 live births)	34.6	39	31
Infant Mortality Ratio (deaths per 1000 live births)	119.9	95	52
Under-5 Mortality Ratio (deaths per 1000 live births)	212	149	74
% literate females age 15-49 years old	*NA*	89.8%	84.9%
DTP3 Coverage 12-23 months	86%	77%	86.4%

Data for this table come from the KEMRI/CDC database (Gem District Column) and Kenya National Bureau of Statistics (KNBS), ICF Macro. Kenya demographic and health survey 2008-2009. 2010;Calverton, Maryland:KNBS and ICF Macro (KDHS, 2009)

Table 3.2 Content of short message system (SMS) for enrollment and reminders in the Mobile Solutions for Immunization (M-SIMU) trial

Message Type	Message Timing	Control	SMS Reminders Only	75 KSH	200 KSH
Enrollment message	Enrollment	Thank you for enrolling Baby <FName> to the KEMRI/CDC M-SIMU study. The greatest wealth is health.	Thank you for enrolling your child in the KEMRI/CDC M-SIMU study. You will get periodic reminders for Baby <Baby FName>'s vaccinations. The greatest wealth is health.	Thank you for enrolling your child in the KEMRI/CDC M-SIMU study. You will get periodic reminders for Baby < Baby FName >'s vaccinations. The greatest wealth is health.	Thank you for enrolling your child in the KEMRI/CDC M-SIMU study. You will get periodic reminders for Baby < Baby FName >'s vaccinations. The greatest wealth is health.
3 day reminder message **Pentavalent 1**	DOB + 6 weeks – 3 days	No message	Tell Mama<Baby FName> that Penta-1 vaccine is due this week. <Motivational Message>	Tell Mama <Baby FName> that Penta-1 vaccine is due this week. You get 75ksh if Baby vaccinated in next 2 weeks. <Motivational Message>	Tell Mama<Baby FName> that Penta-1 vaccine is due this week. You get 200ksh if Baby vaccinated in next 2 weeks. <Motivational Message>
1 day reminder message **Pentavalent 1**	DOB + 6 weeks – 1 day	No message	Tell Mama <Baby FName> that Penta-1 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mama < Baby FName > that Penta-1 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mama<Baby FName> that Penta-1 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>
3 day reminder message **Pentavalent 2**	DOB + 10 weeks – 3 days	No message	Tell Mama<Baby FName> that Penta-2 vaccine is due this week. <Motivational Message>	Tell Mama<Baby FName> that Penta-2 vaccine is due this week. You get 75ksh if Baby vaccinated in next 2 weeks. <Motivational Message>	Tell Mama<Baby FName> that Penta-2 vaccine is due this week. You get 200ksh if Baby vaccinated in next 2 weeks. <Motivational Message>
1 day reminder message **Pentavalent 2**	DOB + 10 weeks – 1 day	No message	Tell Mama<Baby FName> that Penta-2 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mama<Baby FName> that Penta-2 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mama<Baby FName> that Penta-2 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>

Message Type	Message Timing	Control	SMS Reminders Only	75 KSH	200 KSH
3 day reminder message **Pentavalent 3**	DOB + 14 weeks – 3 days	No message	Tell Mama<Baby FName> that Penta-3 vaccine is due this week. <Motivational Message>	Tell Mama<Baby FName> that Penta-3 vaccine is due this week. You get 75ksh if Baby vaccinated in next 2 weeks. <Motivational Message>	Tell Mama<Baby FName> that Penta-3 vaccine is due this week. You get 200ksh if Baby vaccinated in next 2 weeks. <Motivational Message>
1 day reminder message **Pentavalent 3**	DOB + 14 weeks –1 day	No message	Tell Mama<Baby FName> that Penta-3 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mam <Baby FName> that Penta-3 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mama<Baby FName> that Penta-3 vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>
3 day reminder message **Measles**	DOB + 9 months – 3 days	No message	Tell Mama <Baby FName> that Measles vaccine is due this week. <Motivational Message>	Tell Mama <Baby FName> that Measles vaccine is due this week. You get 75ksh if Baby vaccinated in next 2 weeks. <Motivational Message>	Tell Mama <Baby FName> that Measles vaccine is due this week. You get 200ksh if Baby vaccinated in next 2 weeks. <Motivational Message>
1 day reminder message **Measles**	DOB + 9 months – 1 day	No message	Tell Mama <Baby FName> that Measles vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mama <Baby FName> that Measles vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>	Tell Mama <Baby FName> that Measles vaccine is due this week. Go to the clinic if you haven't already. <Motivational Message>
Motivational Message	Appended on to 3 day and 1 day reminder, randomly generated	No message	1. Vaccines save Kenyan babies lives 2. Most <District: Asembo or Gem> babies get vaccinated, be one of them 3. Baby < Baby FName > is happy when healthy. 4. Vaccines are available now. Motivational message is the same for the 1st and 3rd day reminder of the specific vaccine dose		

Abbreviations: DOB, date of birth; Fname, first name; KSH, Kenyan Schilling;

3.9 Figures for Chapter 3

Figure 3.1 The Mobile Solutions for Immunization (M-SIMU) timeline

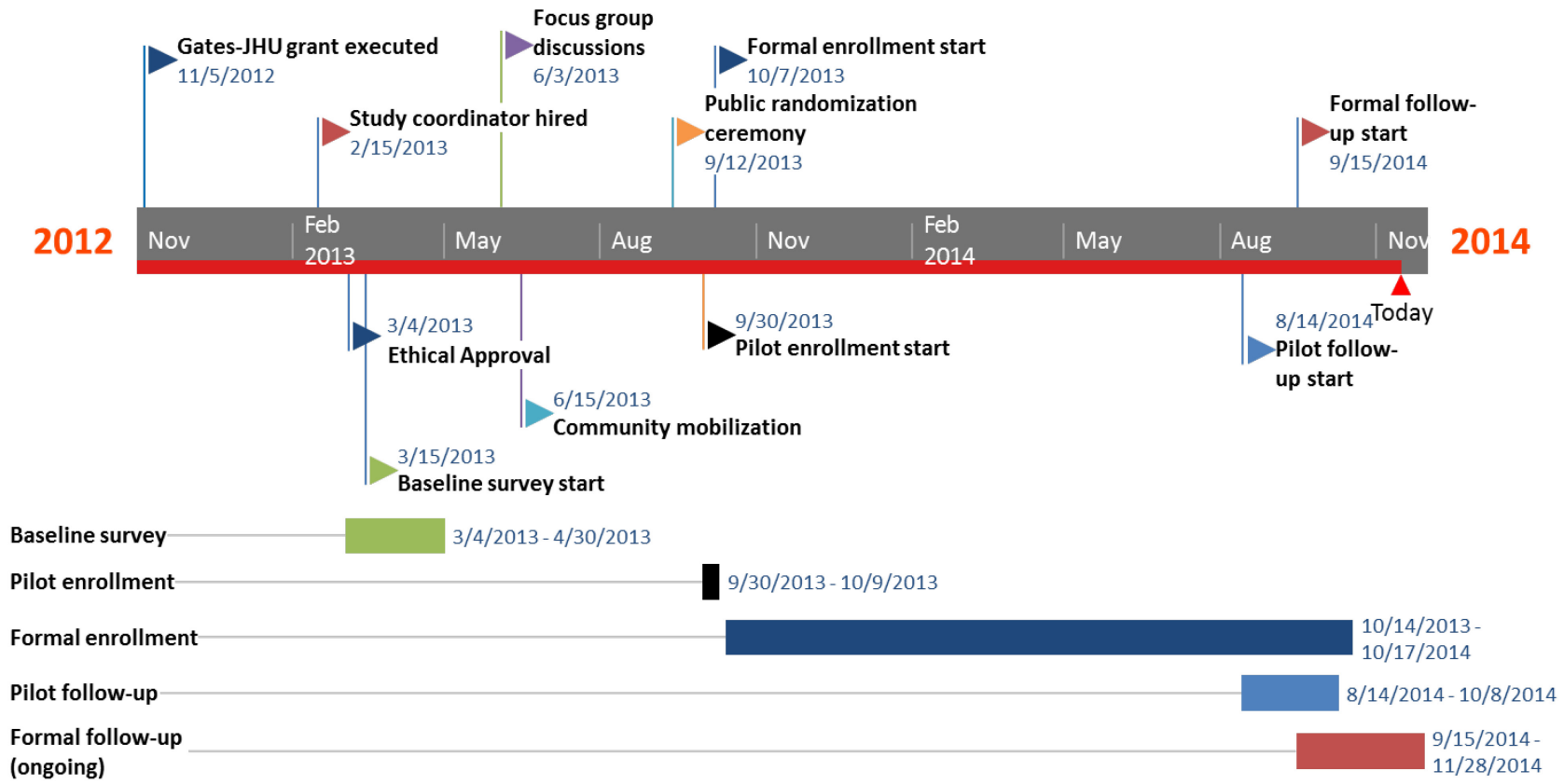
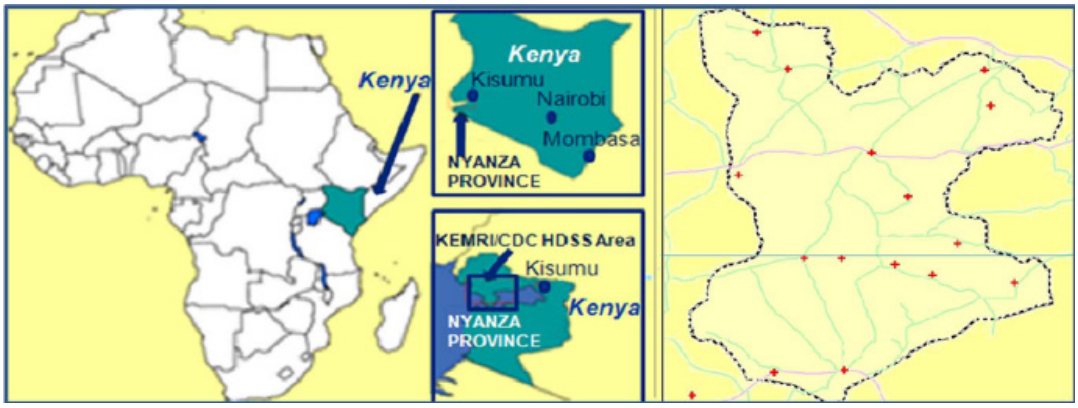


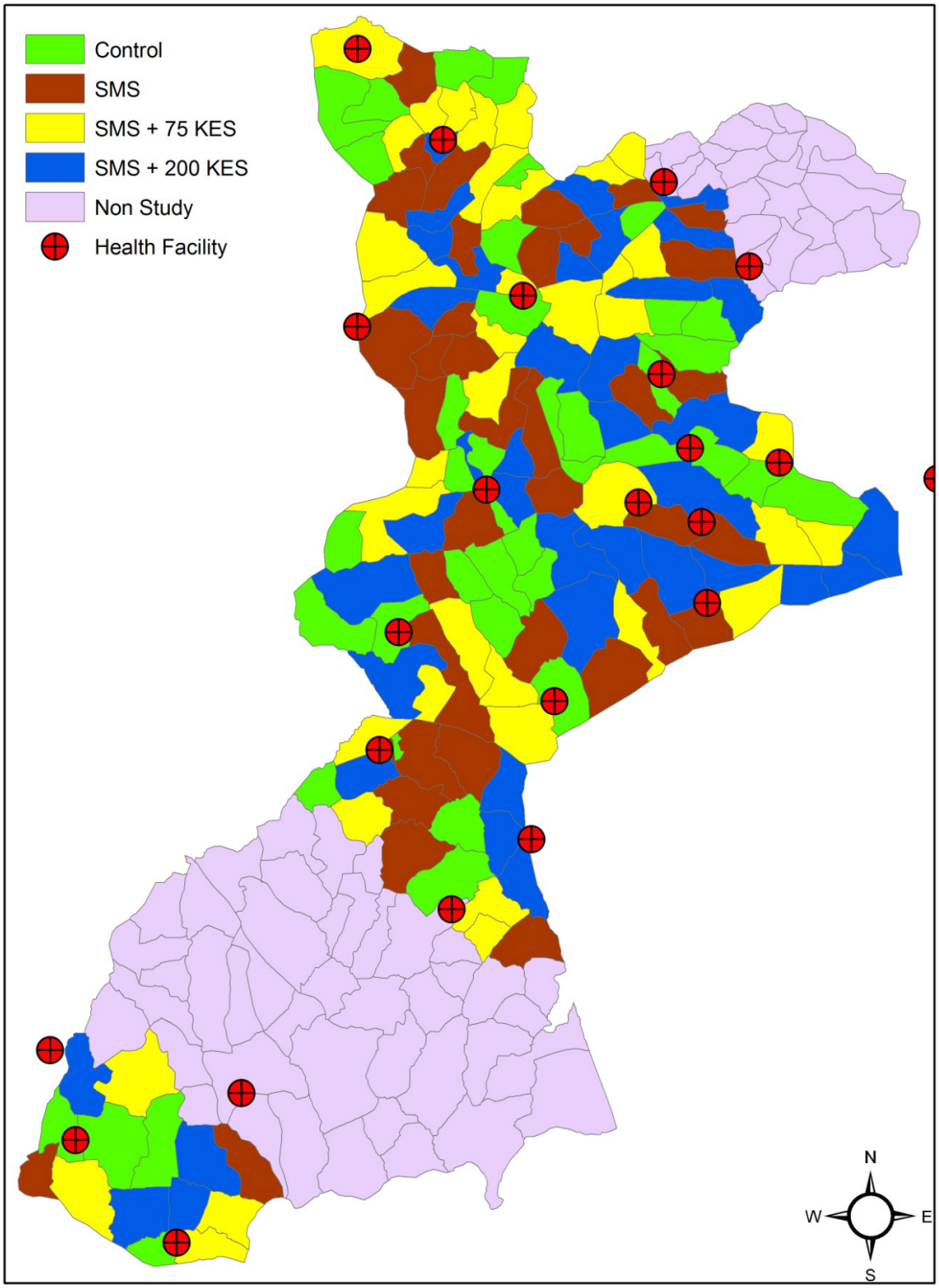
Image courtesy of E. Wangeci Kagucia and the International Vaccine Access Center (IVAC)

Figure 3.2 Maps of study site and health facilities



CAPTION: Red crosses indicate health facilities

Figure 3.3 Villages randomized to study arms and health facilities



Abbreviations: KES, Kenyan Schilling; SMS, short message system

Figure 3.4 Short message system (SMS) and incentive flow diagram

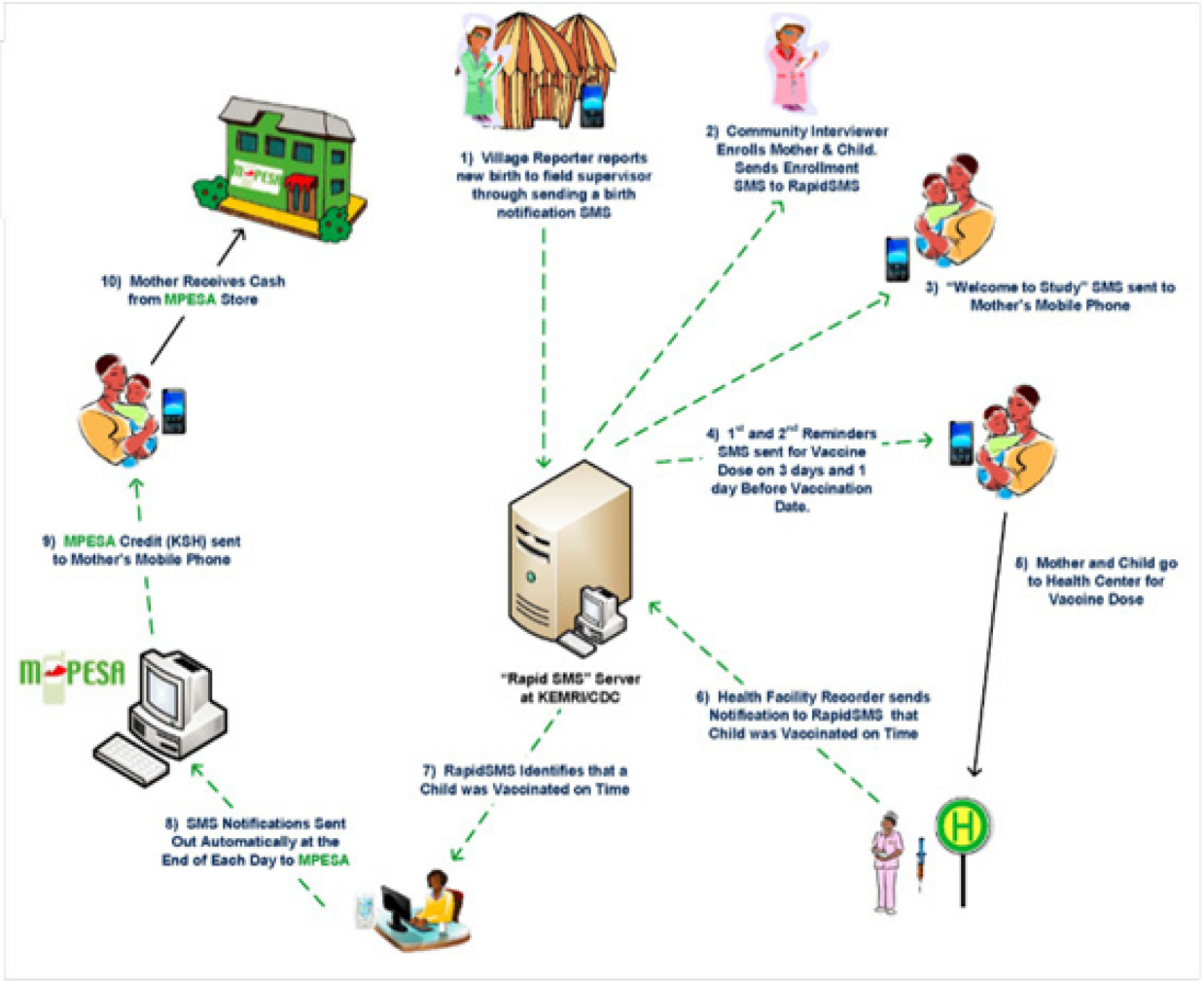
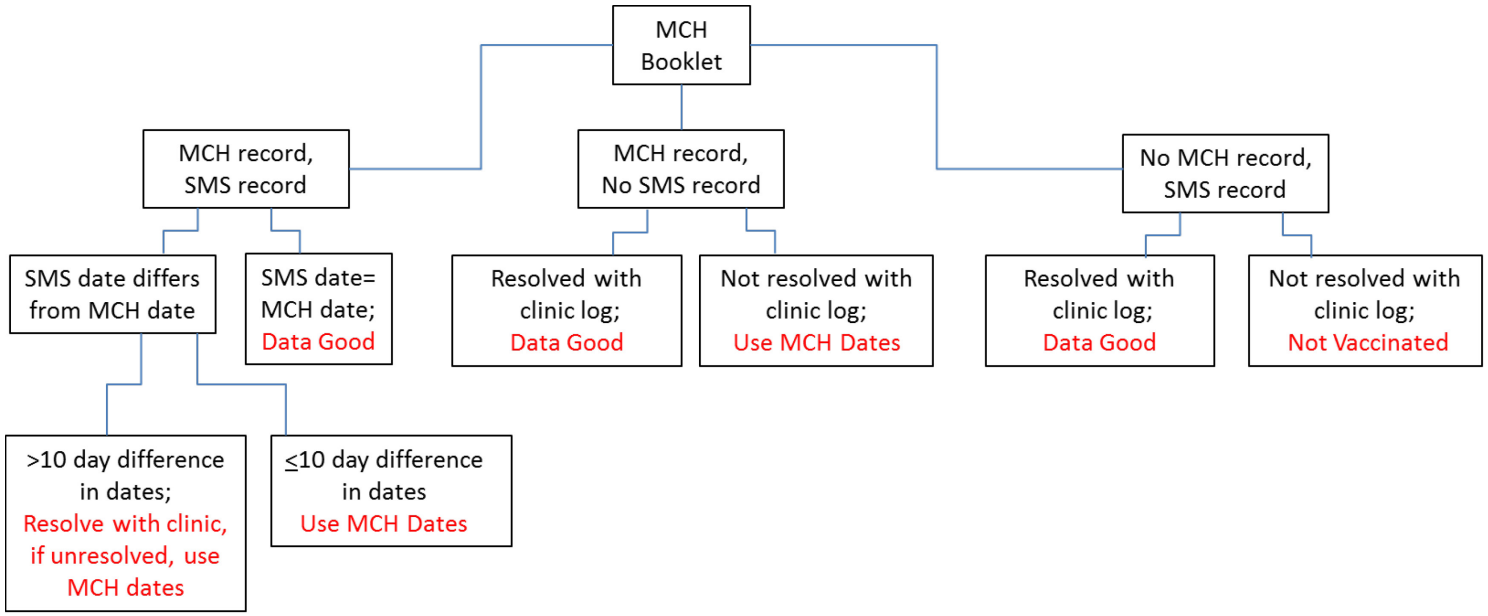


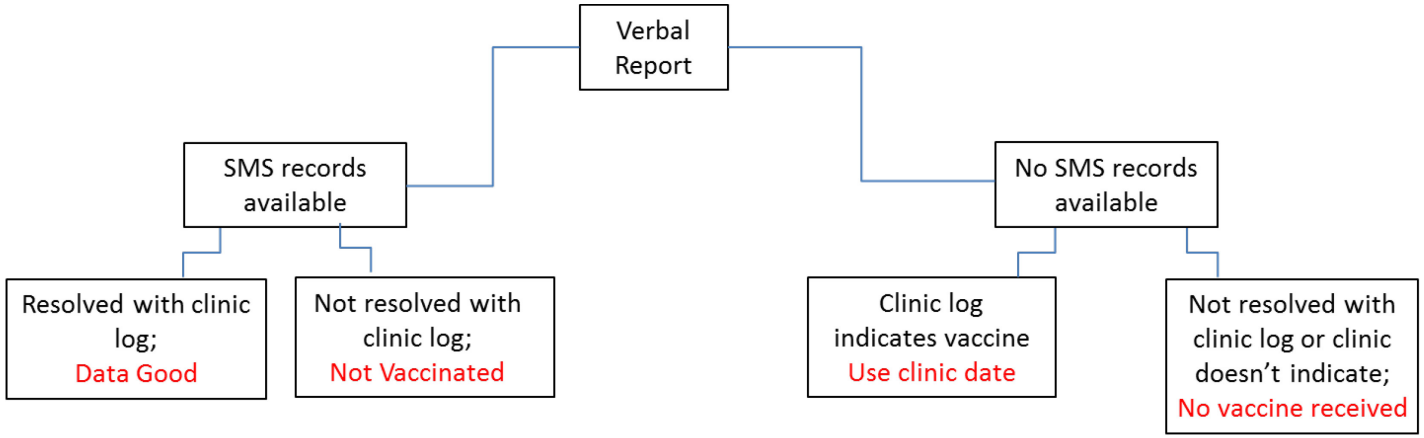
Image from Wakadha, H, et al. The feasibility of using mobile-phone based SMS reminders and conditional cash transfers to improve timely immunization in rural Kenya. *Vaccine.* 2013 Jan 30;31(6):987-93.

Figure 3.5 Determination of immunization status if maternal and child health booklet present at 12 month follow-up



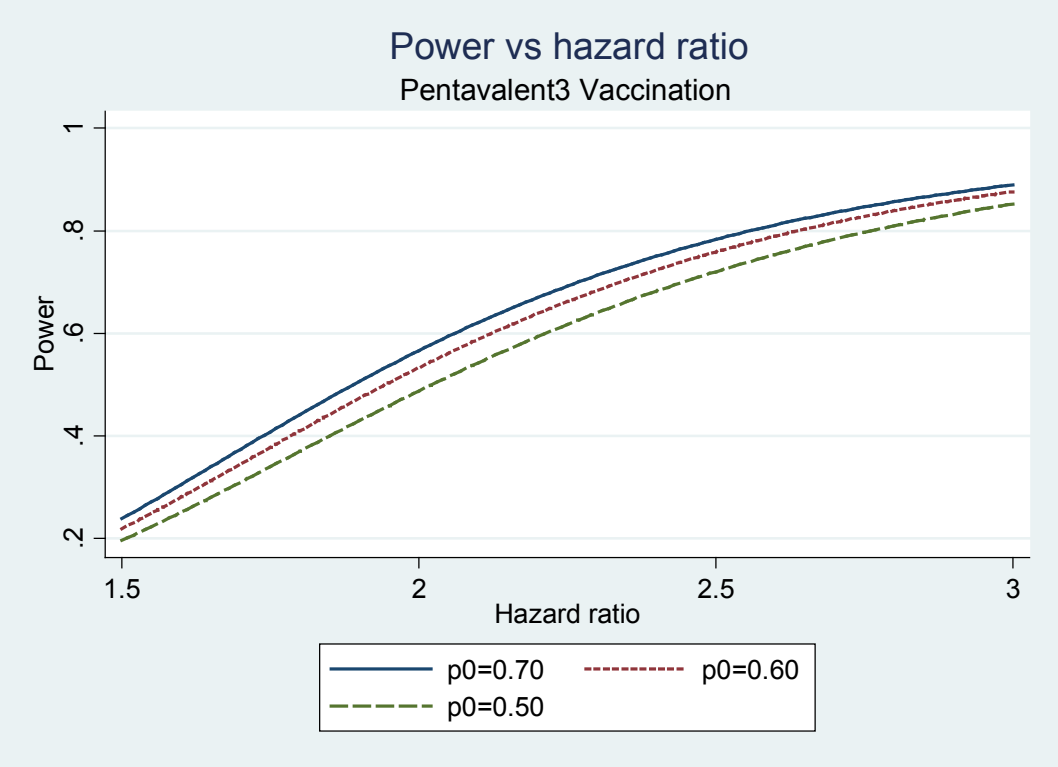
Abbreviations: MCH, maternal and child health booklet; SMS, short message system

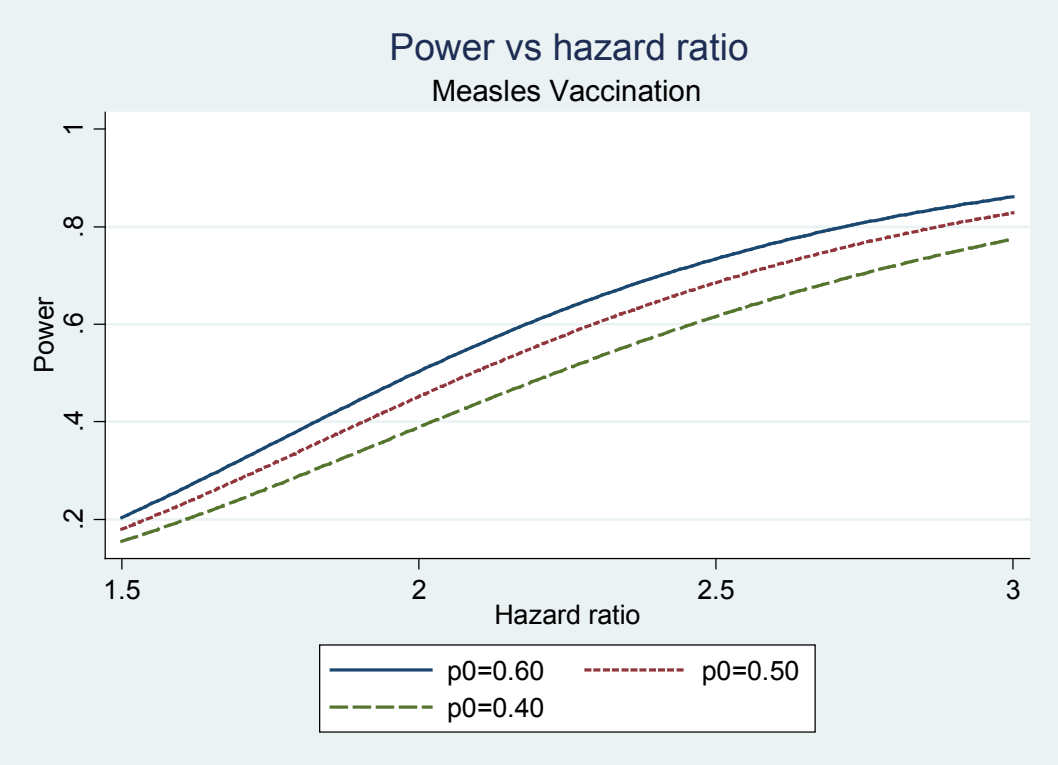
Figure 3.6 Determination of immunization status if verbal report at 12 month follow-up



Abbreviations: SMS, short message system

Figure 3.7 Power calculations for hazard ratios for pentavalent3 and measles vaccination





p0, vaccination coverage of control arm infants at 16 weeks for pentavalent3 and at 286 days for measles vaccines

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Chapter 4. Predictors of non-immunization, delayed immunization, and severely underimmunized infants in rural western Kenya

4.1 Abstract

Objectives: To determine vaccination coverage, timeliness, and underimmunized estimates. To identify risk factors for not being vaccinated, receiving vaccinations with delay, and being severely underimmunized in rural western Kenya.

Methods: In preparation for the Mobile Solutions for Immunizations (M-SIMU) randomized controlled trial, KEMRI/CDC HDSS identified 2632 households with infants aged 12-23 months who were surveyed in March 2013 to ascertain immunization history. Risk factors for delayed, not receiving immunization, and severely underimmunized were calculated using binomial regression with log link and controlling for potential confounders in a sample of 1748 infants who had complete immunization records from the maternal and child health booklet. Infants were considered delayed if immunization was received greater than four weeks from the scheduled date. Severely underimmunized infants were infants that had greater than 90 days of not being immunized cumulatively across five vaccines (BCG, pentavalent1, pentavalent2, pentavalent3, and measles) in the first 12 months of life and also had at least three of the five vaccines delayed.

Results: Immunization coverage for pentavalent1, pentavalent3, measles, and FIC were 99%, 95%, 83%, and 80%, respectively. Older mothers and delayed pentavalent1 vaccine were the only significant predictors common in models of not receiving pentavalent3 or measles vaccine, and not being fully immunized. Infants that received pentavalent1 late (> 4 weeks from scheduled date) were associated with not receiving pentavalent3 (aRR: 5.61; 95%CI: 3.77-8.33), measles vaccine (aRR: 1.51; 95%CI: 1.15-

1.99), and FIC (aRR: 1.87; 95%CI: 1.51-2.32). The proportion of infants with delayed vaccination for pentavalent1, pentavalent3, and measles were 11%, 24%, and 29%, respectively. There were no common risk factors in models of delayed pentavalent1, pentavalent3, and measles vaccines. Approximately 14% of infants were severely underimmunized in the first year of life**.** Older mothers, mothers with lowest levels of education, inability to read English, and not owning a mobile phone were associated with severely underimmunized infants.

Conclusions: Immunization coverage for pentavalent1, pentavalent3, and measles vaccines was high, with lower proportions of timely vaccination and underimmunization. Delayed pentavalent1 receipt was strongly predictive of pentavalent series drop-out and not receiving measles vaccine. Interventions targeted to this subset of population may offer promise in improving immunization coverage.

4.2 Introduction

Vaccines are one of the most cost-effective interventions for increasing childhood survival.[1] The health impact of vaccination, however, is diminished when children do not receive all their vaccines, receive them late, or do not complete the full series of one or more vaccines– all of which are still problems in Africa. Despite the lifesaving potential of vaccines, in 2012 approximately 17% of children, or about 23 million infants, did not complete the three dose sequence of pentavalent vaccine.[2]

In Kenya, the Division of Vaccine and Immunization (DVI) recommends infants receive bacillus Calmette–Guerin (BCG) vaccine at birth, three doses of polio and pentavalent (diphtheria, tetanus toxoid, pertussis, hepatitis B, and *Haemophilus influenzae Type B* antigens) vaccines at 6, 10, and 14 weeks of age, and measles vaccine at 9 months of age.[3] Kenya included the pneumococcal conjugate vaccine (PCV) and rotavirus vaccine in their national immunization plan in 2011 and 2014, respectively.

Coverage estimates for three doses of pentavalent (pentavalent3), or in countries where pentavalent is not available, DTP3 (3 doses of diphtheria, tetanus toxoid, and pertussis antigen containing vaccine) in children 12-23 months old is a common indicator of the strength of a country's immunization system to deliver vaccines.[4, 5] Data from successive Kenyan Demographic and Health Surveys (DHS) found improvements in DTP3 coverage from 72% in 2003, to 86% in 2009.[6] Study site specific estimates for Gem District, Nyanza Province, Kenya found DTP3 coverage estimates to be 55% in 2003[7] and 88% in 2011.[8]

As global DTP3 coverage estimates have improved over time[5, 9], focus is shifting from antigen-specific coverage estimates towards the concept of a fully immunized child

(FIC).[10] Traditionally, a fully immunized child is an infant receiving BCG, 3 doses of DTP/hepatitis B/polio and 1 dose of measles vaccines. As more vaccines have been made available to lower income countries, pneumococcal, rotavirus, HPV, and rubella vaccines merit inclusion in FIC definitions.

However, an often overlooked aspect of DTP and FIC estimates is the age group for which coverage is being assessed. Although the DTP series is to be completed by 14 weeks of age in most developing countries, DTP vaccination coverage is routinely measured at 12-23 months with no restrictions on age of vaccine receipt. The measurement at this time window does not fully capture delays in vaccine administration.

Timeliness of vaccine receipt is important. First, the diseases which pediatric vaccines protect against often have highest morbidities and mortalities at earlier stages of life. Delays of infant immunization have been associated with increased cases of pertussis[11, 12], hepatitis B[13], and *Haemophilus influenzae* type b.[14] Second, timely vaccination ensures maximal herd immunity[15], thereby protecting those that are too young to be vaccinated, medically contraindicated, or do not produce an immunological response (vaccine failure). Delays in vaccination lessen population coverage and create a pool of susceptible individuals thereby increasing the pathogen's ability to spread and theoretically increasing the risk of exposure.

Vaccination delays are prevalent across lower income countries. Two systematic reviews identified a median delay of 6.2- 6.3 weeks for DTP3 across 76 lower and middle-income countries (10 countries were replicated in both reviews).[16, 17] National estimates of median delay for DTP3 in Kenya were lower, 3.2 weeks in 2003, but 25% of Kenyans had DTP3 delays greater than 7.5 weeks.[17]

The objectives of this study were to: (1) Determine the proportion and predictors of infants not receiving vaccination by antigen; (2) Determine the proportion and predictors of infants receiving vaccinations with delay; and (3) Determine the proportion and predictors of infants severely underimmunized.

4.3 Methods

4.3.1 Context within the M-SIMU trial

During March and April of 2013, a cross-sectional survey was conducted in Gem District, Siaya County, Nyanza Province, Kenya to ascertain immunization coverage in infants 12-23 months old. The primary purpose of this survey was to collect immunization coverage and other variables, such as socioeconomic status and mobile phone ownership, to inform sample size requirements and randomization for the Mobile Solutions for Immunization (M-SIMU) cluster randomized trial.

The study site was nested within the boundaries of KEMRI/CDC Health and Demographic Surveillance System (HDSS). Since 2001, the HDSS has systematically collected information on vital events, migration, disease morbidity and demographics every four months for a population of over 220,000 people.[18] The HDSS has served as a platform for numerous studies and intervention trials, notably including randomized controlled trials to test efficacies of insecticide-treated bed-nets and the rotavirus vaccine.[19, 20]

Gem District was under HDSS surveillance from 2003 to 2010 when financial support for HDSS activities stopped. In January 2013, additional funding was obtained and HDSS activities resumed. During the period when Gem was not under surveillance,

village reporters (VRs) continuously recorded vital events and households were enumerated.

In March and April of 2013, the HDSS provided a census of enumerated DSS consented households with infants aged 12-23 months for 120 villages located in Gem District. Using this list of eligible households, M-SIMU community interviewers approached mothers and caretakers of eligible infants and administered a survey at the participant's household.

The study protocol received ethical clearance from the Scientific Steering Committee (SSC), the KEMRI-Nairobi Ethical Review Committee (ERC; SSC#2409), Johns Hopkins University Bloomberg School of Public Health (deferred); Centers for Disease Control and Prevention (deferred).

4.3.2 **Definitions of independent variables**

Participants self-reported demographic variables were included in regression analyses. These variables included number of children under 5 years old that slept in the house last night, the number of people regularly in the household, marital status, socioeconomic status, maternal age, number of maternal education years attempted, mother's ability to read English, infant's age, infant's sex, and maternal mobile phone ownership. Data collected as continuous variables were categorized based on interpretability and relevancy to previous studies. Maternal age was categorized into mothers aged 15-24 years, 25-29 years, and greater than 30 years. Maternal education was grouped into 0-8 years of education attempted, 9-12 years, and greater than 12 years. Child's age was categorized into infants aged 12-18 months and infants aged greater than 18 months. Socioeconomic status was calculated by KEMRI/CDC staff using principal

components analysis from data collected using the KEMRI/CDC DSS Household Socio-economic Form. These variables included occupation, drinking water treatment, type of cooking fuel, and household possessions including livestock. Socio-economic status was provided in quintiles and collapsed to lower 40% and upper 60% for present analysis. Straight-line distances from a child's household to the nearest health facility were calculated using ArcView Geographic Information Systems (GIS; Esri, Redlands, CA). Distance to clinic was categorized into infants living less than or equal to 2 kilometers from the health facility and infants living greater than 2 kilometers from the health facility.

4.3.3 **Definitions of dependent variables**

The three primary outcomes for regression analyses were: (1) not receiving vaccination; (2) delayed vaccination; and (3) severely underimmunized. Non-vaccination and delayed vaccination estimates were restricted to pentavalent1 (delayed only), pentavalent3, measles vaccine, and fully immunized child (FIC), defined as receiving BCG, three doses of polio vaccine, three doses of pentavalent vaccine, and one dose of measles vaccine. Non-vaccination was the proportion of infants from the full sample that had not received a particular vaccination when surveyed at ages 12-23 months of age. Non vaccination estimates were independent of timeliness. The converse, vaccination coverage, was defined as the proportion of infants from the full sample that received the vaccination. Not achieving FIC was defined as the proportion of infants from the full sample that had not received one or more of the eight vaccines by the time of survey. FIC coverage was the proportion of infants that received all eight vaccinations.

Delayed vaccination was defined as the proportion of infants that were immunized greater than four weeks from the DVI recommended schedule. For pentavalent1 and pentavalent3, a vaccine was delayed if received after 10 and 18 weeks, respectively. Delayed measles was defined as receiving measles after 302 days of age. FIC was considered delayed if the infant received all eight vaccines but at least one vaccination was received after 12 months of age, while timely FIC was defined as infants that receive all eight EPI vaccines by 12 months of age. Timely vaccination was defined as the proportion of infants that were immunized within four weeks of the recommended schedule. The denominator for delayed and timely proportions was the number of infants that were immunized, irrespective of timeliness, for the particular vaccine of the estimate.

Severely underimmunized infants were defined as the proportion of infants that were underimmunized for greater than 90 days in the first 12 months of life and were delayed for three of five vaccines (BCG, pentavalent1, pentavalent2, pentavalent3, and measles). Underimmunized infants were defined as infants that neither received the vaccine nor received the vaccine within four weeks of the scheduled date. Infants were not severely underimmunized if the total number of days underimmunized was less than 90 days or if less than three vaccines were received with delay.

4.3.4 **Data Collection and Analysis**

Community interviewers were provided simple, smart-phones (Huawei Y200) employing the ODK application to conduct and collect survey data (Appendix 1). Skip patterns and quality checks were programmed into ODK to help minimize potential errors in data entry and analysis. Staff visited HDSS identified households and asked the compound head if they could interview the caregiver of the child between the ages of 1

and 2 years. Staff members then asked the caregiver if the maternal and child health (MCH) booklet was available, and if so, immunization dates were entered into the mobile-phone based survey. If no MCH booklet was present, staff collected immunization history through verbal report (data excluded from present analysis). Data were cleaned continuously after data entry and missing or questionable data points were relayed back to field staff for follow-up visits.

For the delayed primary outcome, the age at which the vaccine was received was calculated by subtracting the child's date of birth from the date of vaccination. Ages of vaccination were then dichotomized into delayed and timely as described above. Inverse Kaplan-Meir curves were created to graphically depict timeliness of vaccination as performed elsewhere.[21-23] Infants were censored at age immunized or at the age of survey if vaccination was not received.

For the severely underimmunized outcome, infants were censored at 12 months of age. The definition of delayed immunizations used in the delayed outcome was applied to count the number of days delayed. If infants did not receive vaccination, the age at which delays started to accumulate was subtracted from 365 days. The maximum number of days underimmunized for BCG, pentavalent1, pentavalent2, pentavalent3, and measles were, respectively, 337 days, 295 days, 267 days, 239 days, and 62 days. Infants could be cumulatively underimmunized at most for 337 days. If infants received vaccination within 4 weeks of scheduled date, they were given 0 days underimmunized for that vaccine

For BCG, pentavalent1-3, and measles vaccines, the number of days delayed and the number of days the infant was not vaccinated were summed to produce the total

number of days underimmunized. Days underimmunized were not double counted if underimmunized vaccines overlapped. For example, if an infant did not receive BCG and measles vaccine, but received all other vaccines on time, the infant would be underimmunized 337 days for BCG (365-28 days) and 62 days for measles (365-302; where 302=10 months). In total, this infant would be considered underimmunized for 337 days as measles overlapped with BCG. The number of vaccines infants either received with delay or were not given was summed. Infants with 3 or more vaccines that were delayed or not given were considered severely underimmunized if the total number of days underimmunized was greater than 90 days.

Crude risk ratios with 95% confidence intervals for each independent variable were obtained by binomial regression with log link function. For primary objective 1, infants that were not vaccinated were compared to infants that were vaccinated. Primary outcome 2 compared infants that received delayed vaccinations with infants that were timely vaccinated. Primary outcome 3 compared infants with severe underimmunization to all other infants. Final adjusted models were created using forward-stepwise selection of variables with an alpha of 0.05. Analyses were performed using STATA/IC, version 11.2 (Stata Corp, College Station, Texas) and used an alpha of 0.05 for all hypothesis testing.

4.4 Results

A total of 2632 households with infants aged 12-23 months were visited. Excluded from present analysis are 9 (0.3%) infants with unknown birthdate, 66 (2.5%) infants not within 12-23 months, 747 (28.4%) infants with no immunization booklet, and 64 (2.4%) infants with illegible or incomplete immunization records. In total, the final sample

contained 1746 infants aged 12-23 months with complete vaccination history from the immunization booklet. Approximately half of sampled mothers were younger than 25 years old, forty percent completed primary education, ninety percent could read English with difficulty or easily, and over fifty percent of mothers owned a mobile phone (Table 4.1). The average household size was 4 individuals, with the majority of mothers having 1 or 2 infants aged less than five years old in the house. The median straight line distance to the nearest clinic was about 2 kilometers.

4.4.1 **Vaccination Coverage**

Antigen-specific vaccination coverages measured at 12-23 months were high for all individual vaccines (Table 4.2). Approximately 95% of infants received pentavalent3 vaccine, independent of timeliness. Socio-demographic variables significant for predicting infants not receiving pentavalent3 in crude analyses included mothers aged greater than 30 years as compared to mothers aged 15-24 years old (RR: 2.26; 95%CI: 1.43-3.59); households with two children younger than five years old as compared to households with one children under five years old (RR: 1.54; 95%CI: 1.00-2.36), households with more residents (RR: 1.65; 95%CI: 1.11-2.46), and receiving pentavalent1 four weeks late from the scheduled date (RR: 6.32; 95%CI: 4.28-9.35; Table 4.3). Variables associated with receiving pentavalent3 included mothers with 9-12 years of education as compared to those with less than 9 years (RR: 0.56; 95%CI: 0.37-0.87), ability to easily read English as compared to those who cannot (RR: 0.38; 95%CI: 0.22-0.66) and maternal mobile phone ownership (RR: 0.50; 95%CI: 0.34-0.75). There was no association between child's gender, distance to the clinic, and socioeconomic status with pentavalent3 receipt.

In multivariable analyses, mothers aged 25-29 years (aRR: 1.73; 95%CI: 1.04-2.89) and greater than 30 years (aRR: 1.99; 95%CI: 1.23-3.22) and delayed pentavalent1 vaccination (aRR: 5.61; 95%CI: 3.77-8.33) were significantly associated with not receiving pentavalent3 vaccine (Table 4.3). Maternal mobile phone ownership (aRR: 0.52; 95%CI: 0.34-0.78) was associated with infants receiving pentavalent3 vaccine.

Eighty-three percent of infants received measles vaccine (Table 4.2). Determinants of measles vaccination in crude analyses were similar to pentavalent3 except for the addition of mothers in polygamous marriages as compared to single or divorced mothers (RR: 1.60; 95%CI: 1.05-2.42) and older infants (RR: 0.72; 95%CI: 0.58-0.89; Table 4.3). Mothers greater than 30 years old as compared to mothers aged 15-24 years (RR: 1.53; 95%CI: 1.21-1.95), households with 2 infants younger than five years old as compared to those with 1 infant (RR: 1.39; 95%CI: 1.10-1.75), households with more residents (RR: 1.29; 95%CI: 1.05-1.59), and receiving pentavalent1 four weeks late from the scheduled date (RR: 1.63; 95%CI: 1.23-2.15) were predictive of not receiving measles vaccine. Variables associated with measles vaccine receipt include mothers with 9-12 years of education as compared to those with less than 9 years (RR: 0.64; 95%CI: 0.51-0.80); ability to easily read English as compared to not being able to read (RR: 0.58; 95%CI: 0.42-0.81); and maternal mobile phone ownership (RR: 0.76; 95%CI 0.62-0.94). Child's gender, distance to the clinic, and socioeconomic status were not associated with measles vaccination in crude analyses

In multivariable analyses, mothers aged greater than 30 years (aRR: 1.38; 95%CI: 1.08-1.76), households with 2 children under five years old (aRR: 1.34; 95%CI: 1.06-1.70), and infants with delayed pentavalent1 vaccination (aRR: 1.51; 95%CI: 1.15-1.99)

were significantly associated with not receiving measles vaccine (Table 4.3). A mother's ability to easily read English (aRR: 0.67; 95%CI: 0.48-0.94) and older infants (aRR: 0.71; 95%CI: 0.58-0.88) were associated with receiving measles vaccine.

The proportion of infants that were fully immunized with BCG, three doses of polio, three doses of pentavalent, and measles vaccine was 80% (Table 4.2). Crude analyses found a pattern of variables associated with not being fully immunized similar to those associated with not receiving measles or pentavalent3. Socio-demographic variables significantly associated with not being fully immunized include mothers aged greater than 30 years as compared to those 15-24 years old (RR: 1.46; 95%CI: 1.18-1.81), households with 2 infants less than five years old as compared to those with 1 infant (RR: 1.34; 95%CI: 1.10-1.66), households with more residents (RR: 1.30; 95%CI: 1.08-1.57), and delayed pentavalent1 vaccination (RR: 2.06; 95%CI: 1.65-2.56). Variables associated with fully immunized infants in crude analyses included mothers with 9-12 years of education and greater than 12 years as compared to those with less than 8 years, respectively, (RR: 0.67; 95%CI 0.55-0.83) and (RR: 0.59; 95%CI: 0.35-0.99); ability to easily read English as compared to not being able to read (RR: 0.55; 95%CI: 0.41-0.73), maternal mobile phone ownership (RR: 0.74; 95%CI: 0.61-0.89), and older infants (RR: 0.78; 95%CI: 0.65-0.94). Similar to pentavalent3 and measles, child's gender, distance to the clinic, and socioeconomic status were not associated with failure to be fully immunized.

In multivariable analyses, statistically significant variables associated with not being fully immunized included mothers aged greater than 30 years as compared to those 15-24 years old (aRR: 1.28; 95%CI: 1.02-1.59), household with 2 children under 5 years

old (aRR: 1.27; 95%CI: 1.03-1.57), and delayed pentavalent1 vaccination (aRR: 1.87; 95%CI: 1.51-2.32). Factors associated with fully immunized infants include mother's ability to easily read English as compared to not being able to read (aRR: 0.75; 95%CI: 0.53-0.99), maternal mobile phone ownership (aRR: 0.83; 95%CI: 0.68-0.99), and older infants (RR: 0.79; 95%CI 0.66-0.95).

4.4.2 **Vaccination Timeliness**

When considering timely receipt of immunization, antigen-specific estimates are notably lower than their coverage estimates at 12-23 months with BCG, pentavalent3, and measles the most likely to have delays (Table 4.2). The median age of BCG vaccination was two weeks (IQR: 1-5weeks) and for the 31% of infants that received BCG late (>4 weeks of age), the median length of delay was three weeks (IQR: 1-7 weeks; Figures 4.1 and 4.2). For pentavalent1, the median age of vaccination was six weeks (IQR: 6-7 weeks) with a median delay of three weeks (IQR: 1-7 weeks) in the 11% of infants who were delayed. For pentavalent3 and measles, the median ages of receipt were, respectively, 16 weeks (IQR: 15-18weeks) and 41weeks (IQR: 39-44weeks). Of the 24% that had delayed pentavalent3, the median length of delay was three weeks (IQR: 1-9weeks) and for the 29% of measles vaccines administered late, the median delay was four weeks (IQR: 1-9weeks).

The results of regression analyses for factors associated with delayed vaccination are presented in Table 4.4. Socio-demographic variables significantly associated with pentavalent1 delay in crude analyses include mothers aged greater than 30 years as compared to those younger than 25 years (RR: 1.66; 95%CI: 1.20-2.32), polygamous marriage as compared to singled or widowed mothers (RR: 1.81; 95%CI: 1.07-3.08),

households with three or more children under five years old as compared to households with 1 infant under five years of age (RR: 1.59; 95%CI: 1.06-2.40), and households with more residents (RR: 1.34; 95%CI: 1.01-1.77). Ability to easily read English (RR: 0.58; 95%CI: 0.38-0.90) was associated with timely pentavalent1 vaccination. In multivariable analyses, only mothers aged greater than 30 years as compared to those aged 15-24 years were associated with pentavalent1 delay (aRR: 1.66; 95%CI: 1.20-2.32).

Variables significantly associated with delayed pentavalent3 vaccination in crude analyses included oldest mothers (RR: 1.46; 95%CI: 1.19-1.80); households with 2 or 3 infants younger than five years old, respectively, (RR: 1.50; 95%CI: 1.23-1.83) and (RR: 1.44; 95%CI: 1.10-1.89), larger households (RR: 1.25 95%CI: 1.05-1.49), and older children (RR: 1.31; 95%CI: 1.10-1.57). Mothers with 9-12 years and greater than 12 years of education, respectively, (RR: 0.73; 95%CI 0.61-0.89) and (RR: 0.61; 95%CI: 0.38-0.98) and maternal mobile phone ownership (RR: 0.82; 95%CI: 0.69-0.97) were associated with timely measles vaccination. Multivariable analyses found oldest mothers (aRR: 1.40; 95%CI: 1.15-1.72), households with 2 (aRR: 1.48; 95%CI: 1.21-1.79) or 3 children under 5 years old 2 (aRR: 1.40; 95%CI: 1.07-1.84), and older infants (aRR: 1.36; 95%CI: 1.14-1.62) were associated with delayed pentavalent3. Mothers with 9-12 years of education (aRR: 0.74; 95%CI: 0.62-0.90) was associated with timely pentavalent3 with mothers with greater than 12 years trending towards statistical significance (aRR: 0.62; 95%CI: 0.39-1.01; p value= 0.051).

Delayed measles vaccination was associated with numerous socio-demographic variables in crude analyses (Table 4.4). Oldest mothers (RR: 1.31; 95%CI: 1.08-1.58), households with 3 children younger than five years old (RR: 1.29; 95%CI: 1.02-1.63),

larger households (RR: 1.21 95%CI: 1.03-1.42), farther distances to the clinic (RR: 1.26; 95%CI: 1.06-1.49), and older children (RR: 1.37; 95%CI: 1.16-1.62) were significantly associated with delayed measles vaccination. Mothers with the highest level of maternal education (RR: 0.50; 95%CI: 0.30-0.84); ability to read English easily or with difficulty, respectively, (RR: 0.76; 95%CI: 0.59-0.98) and (RR: 0.65; 95%CI: 0.50-0.83), and maternal mobile phone ownership (RR: 0.85; 95%CI: 0.73-0.99) were associated with timely measles vaccination. Multivariable analyses found that maternal ability to easily read English (aRR: 0.68; 95%CI: 0.53-0.87) was associated with infants receiving timely immunization, with mothers who read English with difficulty trending towards significance (aRR: 0.81; 95%CI: 0.62-1.04). Households with more residents (aRR: 1.20; 95%CI: 1.03-1.41) and older children (aRR: 1.37; 95%CI: 1.16-1.61) were significantly associated with delayed measles vaccination.

Crude analyses of factors associated with delayed FIC found significant risk ratios for mothers with 9-12 years of education as compared to those with less than 9 years (RR: 0.62; 95%CI: 0.42-0.93), maternal mobile phone ownership (RR: 0.68; 95%CI: 0.47-0.99) and older infants (RR: 2.49; 95%CI: 1.63-3.82). In multivariable analyses, only mothers owning a mobile phone (aRR: 0.68; 95%CI: 0.47-0.98) and older infants (aRR: 2.50; 95%CI: 1.63-3.83) were significantly associated with delayed FIC.

Overall, the median number of vaccines delayed per child was 1 (IQR: 0-2), (Table 4.5). Restricting analyses to only those who received at least 1 delayed vaccine, the median number of vaccines delayed per infant was 2 (IQR: 1-4). As infants received fewer vaccines, the proportion of the timely received vaccinations decreased. For example, in infants that received a total of five vaccinations, only 15% of the infants

received all five vaccinations on time. Of the 85% that had at least one of these five vaccines delayed, the median number of vaccines delayed was 3 (IQR: 2-4). In contrast, for the infants that received eight vaccinations, 46% received all eight vaccinations in a timely manner. Of the 54% that had at least one vaccination delayed, infants had a median of two vaccines delayed (IQR 1-4).

4.4.3 **Underimmunized**

Infants were underimmunized on average for 55.7 days, or 16.5% of the time they were age-eligible for vaccination, during their first twelve months of life (Table 4.6). Of the 1086 infants (62.1%) that were underimmunized for at least one vaccine, the average number of days underimmunized was 89.6 days, with 29.8% of infants underimmunized for greater than 90 days. Vaccine-specific estimates for all infants found low average days of underimmunized for BCG (16.5 days), pentavalent1 (5.6days), pentavalent2 (13.1days), pentavalent3 (23.4 days), and measles (18.0 days). When estimates were restricted to those underimmunized for at least one vaccine, vaccine-specific average days underimmunized increased for all vaccines; BCG (51.3 days), pentavalent1 (53.3days), pentavalent2 (73.8 days), pentavalent3 (84.1 days), and measles (44.2 days).

Approximately 14% of infants were severely underimmunized in the first year of life. In crude analyses (Table 4.7), infants severely underimmunized were more likely to have mothers aged 25 to 29 years old (RR: 1.39; 95%CI: 1.01-1.93) or greater than 30 years old (RR: 2.51; 95%CI: 1.90-3.32), as compared to mothers 15-24 years old and to live in households with more residents (RR: 1.62 95%CI: 1.27-2.07). Mothers with 9-12 years of education (RR: 0.54; 95%CI: 0.41-0.70) and greater than 12 years of education (RR: 0.25; 95%CI: 0.09-0.66) were less likely to have severely underimmunized infants

than those with less than 9 years of education. Mother's ability to read English easily or with difficulty, respectively, (RR: 0.35; 95%CI: 0.25-0.49) and (RR: 0.60; 95%CI: 0.44-0.82), and maternal mobile phone ownership (RR: 0.58; 95%CI: 0.46-0.74) were associated with infants not being severely underimmunized.

Multivariable analyses found several factors associated with severely underimmunized infants. Mothers 25-29 years old (aRR: 1.46; 95%CI: 1.06-2.02), and greater than 30 years old (aRR: 2.27; 95%CI: 1.71-3.02), as compared to mothers less than 25 years old, were more likely to have infants severely underimmunized. Mothers with 9-12 years of education (aRR: 0.70; 95%CI: 0.53-0.94) and greater than 12 years of education (aRR: 0.37; 95%CI: 0.14-0.99) were less likely to have severely underimmunized infants than those with less than 9 years of education; with a trend towards significance in mothers educated for more than 12 years. A mother's ability to read English easily (aRR: 0.61; 95%CI: 0.42-0.86) and mobile phone ownership (aRR: 0.63; 95%CI: 0.49-0.81) were also significantly associated with infants not severely underimmunized. Additional analyses of risk factors for severely underimmunized infants are located in Appendix 8. In these analyses, where the comparator group was infants that received all vaccinations in a timely manner, risk factors identified were similar to those where comparator group was infants not severely underimmunized.

4.5 Discussion

Immunization coverage levels in our study site have vastly improved since 2003, likely a result of the renewed global commitment to improving immunization delivery systems. Pentavalent3, measles, and FIC 2003 coverage estimates were 68%, 50%, and 41%, respectively.[7] Our 2013 survey found these vaccination coverage estimates

increased to, and correspondingly, 94%, 83%, and 80%. Our vaccination coverage estimates for BCG, pentavalent1, pentavalent3, measles and FIC were very similar to the estimates obtained by others during a survey of the present study site in September 2011[8] which suggests that immunization coverage levels may be plateauing in rural western Kenya. Importantly, pentavalent1 coverage levels were nearly 100%. We chose not to analyze its predictors because of the high coverage. The near uniform population coverage of pentavalent1 may make identification of predictors difficult and, more importantly, a moot point as neither intervention nor programs are needed to target a particular subset of the population that is not receiving pentavalent1.

In regards to predictor variables associated with receipt of pentavalent3, measles, and FIC, each model produced a signature panel of significant predictor variables specific to that vaccine. Older infants were 21 to 29% less likely to achieve FIC or be vaccinated for measles. This finding was expected as there was no age cutoff for coverage, therefore giving older children at the time of the survey a longer time window to be vaccinated. Maternal mobile phone ownership was significantly associated with pentavalent3 and FIC receipt in adjusted models and was significant for measles vaccination in bivariate analysis. This finding is supported by informal discussions with staff from several health facilities staff where nurses have described their efforts to call the mothers of infants that are defaulting on their pentavalent3 sequence. Higher levels of maternal education was only associated with pentavalent3, measles vaccine and fully immunized infants in bivariate analyses. The literature evaluating maternal education and vaccination coverage is inconsistent in lower-income countries; some studies have shown a link of higher education to vaccination[24-26], while others have found that higher education is

associated with lower coverage, where it has been theorized that educated mothers are more likely to have jobs and may be too busy to bring their infant to the clinic.[27] These contrasting findings may be dependent on the population surveyed and how education is categorized. In our analyses, we categorized years of education by completion of primary school (0-8 years), secondary school (9-12 years), and post-secondary education (greater than 12 years).

For pentavalent3, measles, and FIC, delayed pentavalent1 vaccination was the only variable that was statistically significant across all three models and its point estimates were by far the largest. Infants that received pentavalent1 four weeks late were 5.61 (95%CI: 3.77- 8.33) times more likely to not receive pentavalent3 vaccine, 1.51 (95%CI: 1.15-1.99) times more likely to not receive measles vaccine, and 1.87 (95%CI 1.51-2.32) times more likely to not be fully immunized when compared to infants that received pentavalent1 on time. Kaplan-Meier curves of delayed pentavalent1 on pentavalent3 and measles time to vaccination are presented in figure 4.3. In sensitivity analyses where the time window for delays was decreased from four to two weeks, the point estimates slightly decreased while maintaining statistical significance. Briefly, infants that received pentavalent1 two weeks from the scheduled date were 4.90 (95%CI: 3.27-7.34), 1.42 (95%CI: 1.12-1.80), and 1.61 (95%CI: 1.32-1.97) times more likely to not receive pentavalent3, measles, and be fully immunized, respectively. Numerous studies have found that United States infants with delayed first vaccination are at higher risk of not receiving future vaccinations.[28-31] To our knowledge, this is the first demonstration that delayed vaccination positively predicts immunization drop-out in resource-constrained countries.

In the study area, immunization coverage estimates were robust, yet there were significant delays associated with measles and pentavalent3 vaccinations. Although timely vaccination in industrialized countries has been studied for some time[32-36], it is only recently being applied to resource-constrained settings.[7, 17, 22-24, 27, 37-47] In the current study site, the proportion of infants that received timely pentavalent3 and measles vaccination improved from, respectively, 27% and 18% in 2003 to 72% and 59% in 2013. In our sample, adjusted analyses found that infants aged 18-24 months were 36%, 37%, and 150% more likely to have delayed vaccinations for pentavalent3, measles, and fully immunized as compared to infants aged 12 to 17 months. This suggests that even within a one year sampling window, timely immunization is improving. Still, as global immunization coverage levels have markedly improved over the past decade[5, 9], the paradigm must shift from concerns about children being vaccinated, to ensuring vaccinations are now given on time.

The finding that older, less educated mothers, with more children in the household were more likely to have their infant's vaccination delayed has been found in other low-income countries.[24, 27, 37, 40, 45] Although only significant in the delayed FIC model, mothers owning a mobile phone were more likely to have timely vaccinations than those without a mobile phone. As discussed above, this finding may partially be explained by anecdotal accounts of health facility staff calling mothers to remind them of vaccination. Marital status, infant's gender, distance to the clinic, and socioeconomic status were not significant in any of the adjusted models for coverage, delay, or severely underimmunized. Far distances to the clinic have frequently been associated with poor immunization coverage levels.[48-59] Our study site had an average distance of about 2

kilometers to the clinic which may suggest that access is less a barrier to immunization; however, in multiple linear regression analyses of days delayed, distance was significantly associated for pentavalent3 and measles delay (Appendix 9). The lack of association between socioeconomic status and vaccination delay or coverage may be potentially explained due to the overall poverty in this rural site, with little practical differences between the quintiles.

We found that, on average, infants were underimmunized for about two of their first eleven months of life (infants could not be considered underimmunized until age 28 days). In the 62% of infants that were underimmunized for at least one vaccine, the average duration of underimmunization increased to 3 months. For pentavalent3, there was a substantial proportion underimmunized (28%), with a corresponding average of 84 days underimmunized--the longest duration for any of the vaccine-specific estimates. The cumulative number of days underimmunized marries immunization coverage and timeliness estimates, making it a useful estimate to comprehensively examine the magnitude of deficiencies in immunization systems. For measles vaccination, only 53% of infants were immunized by 10 months of age. Although this estimate increased to 72% at 11 months of age, these percentages are concerning, particularly if the delayed and non-immunized are clustered. Measles is a highly contagious virus[60], evidenced by the ability for measles outbreaks to occur in populations comprised of as little as 10% susceptible (i.e. no immune protection).[61] In Kenya, the most recent measles outbreak was in 2011 where 2,461 cases were identified, thus prompting costly, and time-consuming, outreach immunization campaigns.[62]

The risk factors for severely underimmunized were more robust than the separate models for immunization delays and coverage, with the exception of delayed pentavalent1 vaccination in coverage models. Caregivers aged 25-29 years old and caregivers older than 30 years old were, respectively, 46% and 127% more likely to have severely underimmunized infants as compared to caregivers less than 25 years old. Our finding that more educated mothers were less likely to have severely underimmunized infants is consistent with a United States study that examined risk factors for severely delayed infants.[36] Additional studies that examine the magnitude and risk factors of the severely underimmunized are needed from resource constrained countries.

This study has a number of strengths as well as limitations. The first strength is in regards to our sample and its representativeness. By surveying all known caregiver's with eligible infants, selection bias was minimized. Secondly, the high proportion of infants with immunization cards present allowed for a detailed analysis of immunization timeliness. Lastly, risk factors were concurrently identified for immunization coverage, immunization timeliness, and severely underimmunized from a single sample. The majority of previous studies have separately examined either immunization coverage, or, less frequently, immunization timeliness.

A potential limitation is that mothers who provided verbal report of immunization history were not included in analyses because the maternal and child health booklet was missing. This limitation is particularly important if those providing verbal report were less likely to be immunized than those with a maternal and child health booklet. Adjusted analyses for predictors of having immunization booklet present at time of survey as compared to verbal report found that women living closer to the health facility (RR: 0.93;

95%CI 0.88-0.97), younger infants at time of survey (RR: 0.91; 95%CI 0.87-0.96), and male infants (RR: 1.05; 95%CI 1.01-1.10) were more likely to have an immunization card present (Table 4.8). Previous research has found that younger infants, less people in a household, delivery at a health facility, and male infants as factors associated with retention of immunization booklet.[63-65] Because of these differences in socio-demographic characteristics between those with an MCH booklet and those without, it is likely that the vaccination coverage and delay estimates in this study are higher (i.e. more children are vaccinated and more receive timely vaccination) than the true population estimate.

Furthermore, we identified caregivers with infants aged 12-23 months of age through the KEMRI/CDC database. With surveillance activities being just recently resumed in the study site, it is likely that not all of the households had been mapped and interviewed. If these missing households are in more remote regions, it is possible that these infants have lower immunization coverage and increased delays. Therefore, our immunization coverage and timely estimates may be overestimated.

Additional limitations of the present study include a non-comprehensive list of demographic variables that have been found to be associated with immunization coverage and timeliness in other studies. In the study area, community health workers (CHW) are part of a Kenyan national policy to improve the health of child and mother.[66] A previous study found that the quality of interaction with the CHW and the frequency of interaction were significant factors for FIC coverage.[8] Moreover, we had no information on mother's antenatal care seeking behavior and tetanus toxoid immunization[42, 47], paternal characteristics including age and education[37], and place of delivery[23], all of which have

been significant risk factors in other published models. The omission of these variables in our analyses may result in different point estimates and significant factors (i.e. unmeasured confounding bias).

Additionally, our measure of severely underimmunized may not adequately capture the magnitude of underimmunization in the population. To ensure that all infants contributed equal person-time to analyses, it was decided to censor infants at 12 months, which limits the contribution of measles vaccine for underimmunization estimates to 62 days. Future studies would benefit from surveying caregivers of infants greater than 2 years of age to determine if underimmunization persists equally into the second year of life, and to allow measles vaccine opportunity to equally contribute to estimates of cumulative days underimmunized.

Furthermore, only BCG, the pentavalent series, and measles vaccine were included calculations of days underimmunized with the polio vaccine series being omitted. Polio vaccine was omitted from our analysis because it is given at the same time as pentavalent series, with any differences in immunization history of pentavalent and polio doses likely due to vaccine stock-outs or errors in the maternal child and health booklet. In our sample, there was 99% congruency in receiving polio1-3 and pentavalent1-3 vaccines.

Lastly, a potential limitation of the present analyses rests with our definition of timely and delayed vaccination. We defined timely and delayed vaccination as the receipt of vaccine within or after four weeks of the scheduled date as performed in other analyses.[22, 24, 44, 45] However, this arbitrary boundary limit could also then be considered a coverage estimate, albeit at a time point nearer the recommending dosing schedule. An

alternative analysis may have examined days delayed as a continuous variable where days delayed begin to accrue at scheduled date and stop once vaccine is received. One could then tabulate a cumulative measure of 'days delayed', as published elsewhere[36], and which would be more sensitive for detecting timeliness. We opted against this as a main analysis for two reasons. First, very few studies or national immunization surveys have used this measure in their reporting of delay. This would make comparison and generalization of our results to other populations difficult. Our definition of delays as 4 weeks (or 1 month) from the scheduled date is an easily calculated and interpretable statistic that would make it amenable to inclusion in routine immunization reporting systems. Second, there is some ambiguity in the interpretation and clinical ramifications of the results. Is a child with a pentavalent1 delay of 5 days more likely to contract a vaccine preventable illness than an infant with pentavalent1 delay of 10 days? Although this cumulative measure of days delayed may be more sensitive to measuring delay, the clinical implications and correlates are not yet well understood.

Still, as a supplementary analysis (Appendix 9), the results of linear regressions of days delayed for pentavalent1, pentavalent3, and measles vaccines were overall similar, with some minor differences in risk factors significant for delay. For pentavalent1, only mother's English literacy was associated with delay in linear models, while only oldest mothers were significant in the main dichotomous analyses of delayed or timely. Maternal age, number of children under five years old in the house, and infants' age were significant in both linear and dichotomous models of delay. Maternal English literacy, socioeconomic status, and distance to the clinic were significant in only the linear model, with maternal education no longer being significant as found in the dichotomous model.

For measles vaccine, maternal English literacy and age of infant were significant in both models. Distance to the clinic was also significant in the linear model, but not the dichotomous model.

Traditionally, immunization coverage and timeliness have been conceptualized as separate measures. In this study, we created a severely underimmunized variable that combines vaccination delays and not receiving vaccines. Moreover, the distinction between timeliness and coverage is blurred by the finding that timely vaccination (pentavalent1) predicts drop-out of the pentavalent sequence, not receiving measles vaccination, and children not being fully immunized with the eight standard EPI vaccines in resource-limited countries. Although this finding needs to be replicated in other settings, delayed pentavalent1 vaccine could be used as an early warning system to alert practitioners that this infant is at higher risk for drop-out of the EPI schedule. This finding affords several potential interventions that could target early immunization delays to ensure future vaccination.

One solution could be to send short message system (SMS) reminders for future vaccination dates to mothers of infants with delayed pentavalent1. SMS reminders, or text messages, have been found to modestly improve vaccination uptake in the United States.[67-70] Although their efficacy at improving vaccination coverage and timeliness has not been evaluated in resource-constrained countries, aside from a small pilot study[71], the majority of randomized controlled trials in sub Saharan Africa have found SMS reminders improve various forms of healthcare utilization.[72-80] The biggest advantage of employing SMS reminders is that they are relatively inexpensive to send and the process can be easily automated. However, sending SMS reminders is contingent on a literate

population that has high levels of mobile phone ownership. In our study area, literacy levels are high, but only 55% of mothers own a mobile phone with approximately 95% having access to one (Dissertation Chapter 5). The low levels of individual mobile phone ownership would require novel solutions to reach mothers without a mobile phone.

An alternative solution to SMS reminders is the utilization of small incentives paired to timely immunization. Studies conducted in Pakistan and India found that providing food vouchers or provisions conditioned on vaccine receipt markedly improved vaccination coverage.[81, 82] In practice, health facility staff would identify a pentavalent1 delayed infant and inform the mother that for pentavalent2, pentavalent3, and measles doses, she will receive a small incentive (either monetary or food provision) if she brings her infant for future vaccinations. Some may argue against this due to the associated cost of providing payments to mothers. However, the provision of incentives could be cost-neutral, or at best cost-saving, if the incentives dramatically improve vaccination coverage. In Kenya, health facilities hold out-reach campaigns once a month where clinic staff goes into the community to vaccinate for pentavalent series and measles vaccines. If incentives are prompting mothers to go to the clinic for vaccination, the frequency and length of the outreach campaigns would decrease, therefore saving both human and financial resources. Moreover, providing incentives to only those with delay could create a perverse incentive to intentionally delay vaccination in order to receive money.

Lastly, a potential solution to decrease vaccination drop-out in those with delayed pentavalent1 is to provide education on the benefits of vaccination and the potential adverse health outcomes for infants that are not vaccinated. A study in Pakistan found

that health center-based education, lasting approximately two to three minutes, significantly improved completion of the DTP sequence when compared to infants that did not receive such education.[83] This type of approach is advantageous, as compared to the other offered solutions, because it neither requires any technology (i.e. SMS) nor have any financial costs.

In conclusion, vaccination coverage for routinely recommended vaccines in our study area is high. Yet there is a substantial proportion of infants that are being vaccinated after the recommended ages, with a small proportion that are severely underimmunized. Although not often included in reporting of immunization programs, vaccination timeliness is an important measure as those with delays are at higher risk for infection, are more likely to not receive future vaccinations, and lower the population herd immunity. Delayed pentavalent1 receipt was most strongly associated with failure to be immunized in our risk factor analysis. Interventions that target this subset of the population offer promise in improving immunization coverage.

4.6 Tables for Chapter 4

Table 4.1 Socio-demographic characteristics of children aged 12-23 months old with immunization card in Gem District, Kenya

Characteristic	N=1748
Mother's age (years)	
15-24	806 (46.2%)
25-29	474 (27.2%)
≥30	463 (26.6%)
Mother's education (years)	
0-8	934 (54.0%)
9-12	702 (40.6%)
13+	92 (5.3%)
Mother's English reading ability	
Not at all	147 (8.4%)
With Difficulty	631 (36.1%)
Easily	969 (55.5%)
Marital status	
Single/Divorced/Widowed	275 (15.8%)
Monogamous	1279 (73.3%)
Married/Cohabitating	
Polygamous Married/ Cohabitating	192 (11.0%)
Children < 5 years old in house	
≤ 1	708 (40.6%)
2	802 (45.9%)
≥3	236 (13.5%)
Household size (no. of people)	
≤4	920 (52.7%)
>4	827 (47.3%)
Socioeconomic status[1]	
Bottom 40%	713 (41.0%)
Upper 60%	1026 (59.0%)
Mother's mobile phone ownership	
Owns Phone	946 (54.1%)
Has Access/None	802 (45.9%)
Distance to clinic (km)	
≤ 2	729 (42.9%)
>2	970 (57.1%)
Child's age (months)	
12-18	860 (49.2%)
>18 - 24	888 (50.8%)
Child's gender	
Female	827 (47.3%)
Male	921 (52.7%)

[1]Socioeconomic status derived from Principal Components Analysis of household possessions

Table 4.2 Vaccination coverage and timeliness in infants ages 12-23 months old with immunization card in Gem District, Kenya

Vaccine	Delayed Vaccination[1] % (n)	Timely Vaccination[2] % (n)	Coverage 12-23 months % (n)
BCG	31.3% (540)	68.7% (1187)	98.8% (1727)
Polio1	10.5% (182)	89.5% (1556)	99.4% (1738)
Polio2	16.4% (280)	83.6% (1425)	97.5% (1705)
Polio3	24.0% (390)	76.0% (1237)	93.1% (1627)
Pentavalent1	10.2% (176)	89.8% (1564)	99.6% (1740)
Pentavalent2	16.0% (273)	84.0% (1438)	97.9% (1711)
Pentavalent3	23.6% (389)	76.4% (1262)	94.5% (1651)
Measles	29.3% (425)	70.7% (1025)	83.0% (1450)
FIC-12months[3]	7.2% (101)	92.8% (1293)	79.8% (1394)

Abbreviations: BCG, Bacillus Calmette–Guérin vaccine; FIC, full immunization coverage; Polio1, first dose of polio vaccine; Polio2, second dose of polio vaccine; Polio3, third dose of polio vaccine; Pentavalent1, first dose of pentavalent vaccine; Pentavalent2, second dose of pentavalent vaccine; Pentavalent3, third dose of pentavalent vaccine

[1] For individual vaccines, delayed is receiving vaccine greater than 4 weeks from the scheduled date. For fully immunized child (FIC), delayed is receiving all vaccines but at least one of the vaccines was received after 12 months of age

[2] For individual vaccines, timely is receiving vaccine within 4 weeks from the scheduled date. For FIC, timely is receiving all vaccines by 12 months of age

[3] FIC= Fully immunized child and includes BCG, Polio1-3, Pentavalent1-3, Measles

Table 4.3 Bivariate and multivariate analyses for predictors of non-immunized vs those receiving immunization by antigen and for fully immunized children (FIC).

	Pentavalent3 Not Received		**Measles Not Received**		**FIC Not Achieved[1]**	
Mother's age	Crude RR(CI)	Adj RR (CI)	Crude RR (CI)	Adj RR (CI)	Crude RR (CI)	Adj RR (CI)
15-24years	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
25-29years	1.53 (0.92-2.54)	**1.73 (1.04-2.89)**	1.08 (0.83-1.41)	1.06 (0.81-1.39)	1.07 (0.84-1.36)	1.07 (0.84-1.36)
≥30years	**2.26 (1.43-3.59)**	**1.99 (1.23-3.22)**	**1.53 (1.21-1.95)**	**1.38 (1.08-1.76)**	**1.46 (1.18-1.81)**	**1.28 (1.02-1.59)**
Mother's education						
0-8years	*Ref.*		*Ref.*		*Ref.*	*Ref.*
9-12years	**0.56 (0.37-0.87)**		**0.64 (0.51-0.80)**		**0.67 (0.55-0.83)**	0.82 (0.66-1.02)
13+years	0.15 (0.02-1.10)		0.58 (0.33-1.03)		**0.59 (0.35-0.99)**	0.75 (0.43-1.31)
Mother's English reading ability						
Not at all	*Ref.*		*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	0.60 (0.34-1.03)		0.86 (0.62-1.19)	0.96 (0.68-1.33)	0.79 (0.60-1.06)	0.90 (0.68-1.20)
Easily	**0.38 (0.22-0.66)**		**0.58 (0.42-0.81)**	**0.67 (0.48-0.94)**	**0.55 (0.41-0.73)**	**0.75 (0.53-0.99)**
Marital status						
Single/Divorced/Widowed	*Ref.*		*Ref.*		*Ref.*	
Monogamous Married	1.59 (0.83-3.04)		1.36 (0.98-1.90)		1.19 (0.90-1.58)	
Polygamous Married	1.86 (0.83-4.16)		**1.60 (1.05-2.42)**		1.37 (0.95-1.98)	
Children < 5 years old in house						
≤ 1	*Ref.*		*Ref.*	*Ref.*	*Ref.*	*Ref.*
2	**1.54 (1.00-2.36)**		**1.39 (1.10-1.75)**	**1.34 (1.06-1.70)**	**1.34 (1.10-1.66)**	1.27 (1.03-1.57)
≥3	1.16 (0.66-2.22)		1.30 (0.94-1.81)	1.23 (0.89-1.70)	1.27 (0.95-1.71)	1.19 (0.89-1.60)
Household size						
≤4 people	*Ref.*		*Ref.*		*Ref.*	
>4 people	**1.65 (1.11-2.46)**		**1.29 (1.05-1.59)**		**1.30 (1.08-1.57)**	
Socioeconomic status[2]						
Bottom 40%	*Ref.*		*Ref.*		*Ref.*	
Upper 60%	0.74 (0.50-1.09)		0.97 (0.79-1.21)		0.95 (0.78-1.14)	
Mother's mobile phone						
Has Access/None	*Ref.*	*Ref.*	*Ref.*		*Ref.*	*Ref.*
Owns Phone	**0.50 (0.34-0.75)**	**0.52 (0.34-0.78)**	**0.76 (0.62-0.94)**		**0.74 (0.61-0.89)**	**0.83 (0.69-1.00)**
Distance to clinic						
≤ 2km	*Ref.*		*Ref.*		*Ref.*	
>2km	0.99 (0.67-1.47)		1.10 (0.89-1.36)		1.03 (0.85-1.25)	

Child's age						
12-18months	*Ref.*		*Ref.*	*Ref.*	*Ref.*	*Ref.*
>18 – 24months	0.84 (0.57-1.24)		**0.72 (0.58-0.89)**	**0.71 (0.58-0.88)**	**0.78 (0.65-0.94)**	**0.79 (0.66-0.95)**
Child's gender						
Female	*Ref.*		*Ref.*		*Ref.*	
Male	1.46 (0.98-2.17)		1.08 (0.88-1.33)		1.06 (0.88-1.28)	
Pentavalent1 receipt[3]						
On time	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Delayed	**6.32 (4.28-9.35)**	**5.61 (3.77-8.33)**	**1.63 (1.23-2.15)**	**1.51 (1.15-1.99)**	**2.06 (1.65-2.56)**	**1.87 (1.51-2.32)**

Abbreviations: Pentavalent3, third dose of pentavalent vaccine; RR, risk ratio; FIC, full immunization coverage; pentavalent1, first dose of pentavalent vaccine

[1]Child that received BCG, Polio1-3, Penta1-3, and Measles.
[2] Socioeconomic status derived from Principal Components Analysis of household possessions
[3] Delay defined as receiving pentavalent1 four weeks greater than the scheduled date.
Bolded risk ratios and confidence intervals indicate $p<0.05$

Table 4.4 Bivariate and multivariate analyses for predictors of delayed immunization.

	Pentavalent1 delayed[1]		Pentavalent3 delayed[1]		Measles delayed[1]		FIC delayed[2]	
Mother's age	Crude RR (CI)	Adj RR (CI)	Crude RR (CI)	Adj RR (CI)	Crude RR (CI)	Adj RR (CI)	Crude RR (CI)	Adj RR (CI)
15-24 years	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	
25-29 years	1.35 (0.95-1.91)	1.35 (0.95-1.91)	1.22 (0.98-1.51)	1.18 (0.95-1.46)	1.13 (0.93-1.37)		1.23 (0.79-1.94)	
≥30 years	**1.66 (1.20-2.32)**	**1.66 (1.20-2.32)**	**1.46 (1.19-1.80)**	**1.40 (1.15-1.72)**	**1.31 (1.08-1.58)**		1.33 (0.85-2.10)	
Mother's education								
0-8 years	*Ref.*		*Ref.*	*Ref.*	*Ref.*		*Ref.*	
9-12 years	0.89 (0.66-1.19)		**0.73 (0.61-0.89)**	**0.74 (0.62-0.90)**	0.88 (0.75-1.04)		**0.62 (0.42-0.93)**	
13+years	0.82 (0.41-1.62)		**0.61 (0.38-0.98)**	0.62 (0.39-1.01)	**0.50 (0.30-0.84)**		0.00 (0 - ∞)	
Mother's English reading								
Not at all	*Ref.*		*Ref.*		*Ref.*	*Ref.*	*Ref.*	
With Difficulty	0.72 (0.46-1.13)		0.99 (0.73-1.34)		**0.76 (0.59-0.98)**	0.81 (0.62-1.04)	0.80 (0.42-1.50)	
Easily	**0.58 (0.38-0.90)**		0.76 (0.56-1.03)		**0.65 (0.50-0.83)**	**0.68 (0.53-0.87)**	0.57 (0.30-1.06)	
Marital status								
Single/Divorce/Widow	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
Monogamous Married	1.23 (0.80-1.90)		1.13 (0.87-1.56)		1.16 (0.92-1.47)		0.81 (0.50-1.32)	
Polygamous Married	**1.81 (1.07-3.08)**		1.35 (0.96-1.88)		1.34 (0.98-1.82)		1.06 (0.55-2.08)	
Children < 5 years old in house								
≤ 1	*Ref.*		*Ref.*	*Ref.*	*Ref.*		*Ref.*	
2	1.32 (0.96-1.82)		**1.50 (1.23-1.83)**	**1.48 (1.21-1.79)**	1.14 (0.96-1.36)		1.27 (0.83-1.92)	
≥3	**1.59 (1.06-2.40)**		**1.44 (1.10-1.89)**	**1.40 (1.07-1.84)**	**1.29 (1.02-1.63)**		1.50 (0.86-2.61)	
Household size								
≤4 people	*Ref.*		*Ref.*		*Ref.*	*Ref.*	*Ref.*	
>4people	**1.34 (1.01-1.77)**		**1.25 (1.05-1.49)**		**1.21 (1.03-1.42)**	**1.20 (1.03-1.41)**	1.42 (0.98-2.08)	
Socioeconomic status[3]								
Bottom 40%	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
Top 60%	0.90 (0.68-1.20)		0.94 (0.79-1.12)		1.04 (0.89-1.23)		0.79 (0.54-1.14)	
Mother's mobile phone								
Has Access/None	*Ref.*		*Ref.*		*Ref.*		*Ref.*	*Ref.*
Owns Phone	0.81 (0.61-1.07)		**0.82 (0.69-0.97)**		**0.85 (0.73-0.99)**		**0.68 (0.47-0.99)**	**0.68 (0.47-0.98)**
Distance to clinic								
≤ 2 km	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
>2 km	1.04 (0.78-1.39)		1.15 (0.97-1.39)		**1.26 (1.06-1.49)**		1.34 (0.90-2.00)	

Child's age								
12-18 months	*Ref.*		*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
>18 – 24 months	1.06 (0.80-1.41)		**1.31 (1.10-1.57)**	**1.36 (1.14-1.62)**	**1.37 (1.16-1.62)**	**1.37 (1.16-1.61)**	**2.49 (1.63-3.82)**	**2.50 (1.63-3.83)**
Child's gender								
Female	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
Male	1.08 (0.82-1.43)		0.90 (0.76-1.07)		0.92 (0.78-1.08)		1.05 (0.72-1.53)	

Abbreviations: Pentavalent1, first dose of pentavalent vaccine; Pentavalent3, third dose of pentavalent vaccine; RR, risk ratio; FIC, full immunization coverage;

[1] Delayed is vaccination received after four weeks of scheduled date. Reference group is infants that received vaccine within four week of scheduled date
[2] Child that received BCG, Polio1-3, Penta1-3, and Measles. Delay is receiving at least 1 vaccine at age greater than 12 months. Reference group is receiving all 8 vaccines by 12 months of age
[3] Socioeconomic status derived from Principal Components Analysis of household possessions

Bolded risk ratios and confidence intervals indicate $p<0.05$

Table 4.5 Proportions of vaccines given on time and delayed stratified by the number of vaccines received for infants aged 12-23 months in Gem District, Kenya[1]

Number of Vaccines Received	Number of infants	Infants with all timely vaccines N (%)	Infants with ≥1 vaccine delayed N (%)	Infants with delay, Median vaccines delayed (IQR)	All infants, Median vaccines delayed (IQR)
0	1	--------	--------	-------	-------
1	4	4 (100%)	0 (0.0%)	-------	-------
2	2	2 (100%)	0 (0.0%)	-------	-------
3	27	4 (14.8%)	23 (85.2%)	2 (1-3)	2 (1-3)
4	11	3 (27.3%)	8 (72.7%)	2 (1-3.5)	1 (0-3)
5	39	6 (15.4%)	33 (84.6%)	3 (2-4)	2 (1-4)
6	21	1 (4.8%)	20 (95.2%)	4 (2-5)	4 (2-5)
7	249	107 (43.0%)	142 (57.0%)	2 (1-5)	1 (0-3)
8	1394	635 (45.6%)	759 (54.4%)	2 (1-4)	1 (0-2)
Total	1748	762 (43.6%)	986 (56.4%)	2 (1-4)	1 (0-2)

Abbreviation: IQR, Inter-quartile range

[1] The eight vaccines include: BCG, three doses of polio, three doses of pentavalent, measles

Table 4.6 Days underimmunized in first 12 months of life[1]

	All Vaccines[2]		BCG		Penta1		Penta2		Penta3		Measles	
	N (%)	Mean (SE)	N (%)	Mean (SE)	N (%)	Mean (SE)	N (%)	Mean (SE)	N (%)	Mean (SE)	N (%)	Mean (SE)
All Infants	1748	55.7 (2.0)	1748	16.5 (1.2)	1748	5.6 (0.7)	1748	13.1 (1.2)	1748	23.4 (1.5)	1748	18.0 (0.6)
Under-immunized Infants	1086 (62.1)	89.6 (2.8)	561 (32.1)	51.3 (3.2)	184 (10.5)	53.3 (6.0)	310 (17.7)	73.8 (5.3)	486 (27.8)	84.1 (4.1)	713 (40.8)	44.2 (0.8)
Infants underimmunized, n (%)												
0 days	NA		525	(48.3)	902	(83.1)	776	(71.5)	600	(55.3)	373	(34.4)
1-7	126	(11.6)	102	(9.4)	64	(5.9)	68	(6.3)	85	(7.8)	93	(8.6)
8-30	227	(20.9)	215	(19.8)	49	(4.5)	94	(8.7)	136	(12.5)	133	(12.3)
31-60	128	(11.8)	113	(10.4)	30	(2.8)	49	(4.5)	64	(5.9)	76	(7.0)
61-90	282	(26.0)	51	(4.7)	10	(0.9)	21	(1.9)	39	(3.6)	411	(37.9)
91-180	141	(13.0)	47	(4.3)	12	(1.1)	20	(1.8)	49	(4.5)	NA	
181-270	89	(8.2)	6	(0.6)	6	(0.6)	58	(5.3)	113	(10.4)	NA	
271-337	93	(8.6)	27	(2.5)	13	(1.2)	NA		NA		NA	
Total possible delay (days)	337		337		295		267		239		62	

Abbreviations: SE; standard error; NA, not applicable

[1] Underimmunized is the number of days the infant was either unvaccinated or delayed in receiving the vaccine. Underimmunized days started to accumulate four weeks from the scheduled date

[2] All vaccines include BCG, pentavalent1, pentavalent2, pentavalent3, and measles vaccines

Table 4.7 Bivariate and multivariate analyses for predictors of severe underimmunization

Characteristic	Crude RR (CI)	p	Adj RR (CI)	p
Mother's age (yrs)				
15-24	Ref.		Ref.	
25-29	1.39 (1.01-1.93)	0.04	1.46 (1.06-2.02)	0.02
≥30	2.51 (1.90-3.32)	<0.01	2.27 (1.71-3.02)	<0.01
Mother's education (yrs)				
0-8	Ref.		Ref.	
9-12	0.54 (0.41-0.70)	<0.01	0.70 (0.53-0.94)	0.02
13+	0.25 (0.09-0.66)	<0.01	0.37 (0.14-0.99)	0.049
English reading ability				
Not at all	Ref.		Ref.	
With Difficulty	0.60 (0.44-0.82)	<0.01	0.78 (0.57-1.08)	0.14
Easily	0.35 (0.25-0.49)	<0.01	0.61 (0.42-0.86)	<0.01
Marital status				
Single/Divorced/Widowed	Ref.			
Monogamous Married	1.26 (0.88-1.82)	0.21		
Polygamous Married	1.38 (0.86-2.23)	0.18		
Children < 5 years old in house				
≤ 1	Ref.			
2	1.40 (1.08-1.83)	0.01		
≥3	1.31 (0.90-1.90)	0.16		
Household size (no. of people)				
≤4	Ref.			
>4	1.62 (1.27-2.07)	<0.01		
Socioeconomic status[1]				
Bottom 40%	Ref.			
Upper 60%	0.77 (0.61-0.98)	0.03		
Mobile phone ownership				
Has Access/None	Ref.		Ref.	
Owns Phone	0.58 (0.46-0.74)	<0.01	0.63 (0.49-0.81)	<0.01
Distance to clinic (km)				
≤ 2	Ref.			
>2	1.12 (0.88-1.43)	0.35		
Child's age (months)				
12-18	Ref.			
>18 - 24	1.05 (0.83-1.34)	0.66		
Child's gender				
Female	Ref.			
Male	1.05 (0.82-1.33)	0.71		

Abbreviation: RR, risk ratio; yrs, years

[1] Socioeconomic status derived from Principal Components Analysis of household possessions

CAPTION: Severely underimmunized infants had greater than 90 days underimmunized and were delayed for three of five vaccines (BCG, pentavalent1, pentavalent2, pentavalent3, measles). Comparison group was all other infants.

Table 4.8 Comparison of socio-demographic characteristics of children aged 12-23 months old by reporting method in Gem District, Kenya

Characteristic	Card (n=1748)	Verbal (n=689)	Card Present Crude RR (CI)	Card Present Adj RR (CI)
Mother's age (years)				
15-24	806 (46.2%)	340 (50.2%)	Ref.	
25-29	474 (27.2%)	171 (25.2%)	1.04 (0.98-1.11)	
≥30	463 (26.6%)	167 (24.7%)	1.04 (0.98-1.11)	
Mother's education (years)				
0-8	934 (54.0%)	371 (55.5%)	Ref.	
9-12	702 (40.6%)	253 (37.9%)	1.03 (0.75-1.08)	
13+	92 (5.3%)	44 (6.6%)	0.94 (0.84-1.07)	
Mother's English reading				
Not at all	147 (8.4%)	49 (7.1%)	Ref.	
With Difficulty	631 (36.1%)	267 (38.8%)	0.94 (0.86-1.03)	
Easily	969 (55.5%)	372 (54.1%)	0.96 (0.88-1.05)	
Marital status				
Single/Divorced/Widowed	275 (15.8%)	135 (19.7%)	Ref.	Ref.
Monogamous married	1279 (73.3%)	470 (68.6%)	**1.09 (1.01-1.17)**	1.06 (0.99-1.14)
Polygamous married	192 (11.0%)	80 (11.6%)	1.05 (0.95-1.16)	1.02 (0.92-1.12)
Children < 5 years old in house				
≤ 1	708 (40.6%)	341 (49.6%)	Ref.	Ref.
2	802 (45.9%)	248 (36.1%)	**1.13 (1.07-1.19)**	**1.13 (1.04-1.16)**
≥3	236 (13.5%)	98 (14.3%)	1.05 (0.97-1.14)	0.99 (0.91-1.08)
Household size (no. of people)				
≤4	920 (52.7%)	396 (57.6%)	Ref.	Ref.
>4	827 (47.3%)	291 (42.3%)	**1.06 (1.01-1.11)**	1.04 (0.99-1.10)
Socioeconomic status[1]				
Bottom 40%	713 (41.0%)	260 (41.0%)	Ref.	
Upper 60%	1026 (59.0%)	422 (61.9%)	0.97 (0.92-1.02)	
Mobile phone ownership				
Owns Phone	946 (54.1%)	398 (57.8%)	Ref.	
Has Access/None	802 (45.9%)	291 (42.2%)	0.96 (0.91-1.01)	
Distance to clinic (km)				
≤ 2	729 (42.9%)	244 (36.7%)	Ref.	Ref.
>2	970 (57.1%)	421 (63.3%)	**0.93 (0.89-0.98)**	**0.93 (0.88-0.97)**
Child's age (months)				
12-18	860 (49.2%)	282 (40.9%)	Ref.	Ref.
>18 - 24	888 (50.8%)	407 (59.1%)	**0.91 (0.87-0.96)**	**0.91 (0.87-0.96)**
Child's gender				
Female	827 (47.3%)	364 (52.8%)	Ref.	Ref.
Male	921 (52.7%)	325 (47.2%)	**1.06 (1.01-1.12)**	**1.05 (1.01-1.10)**

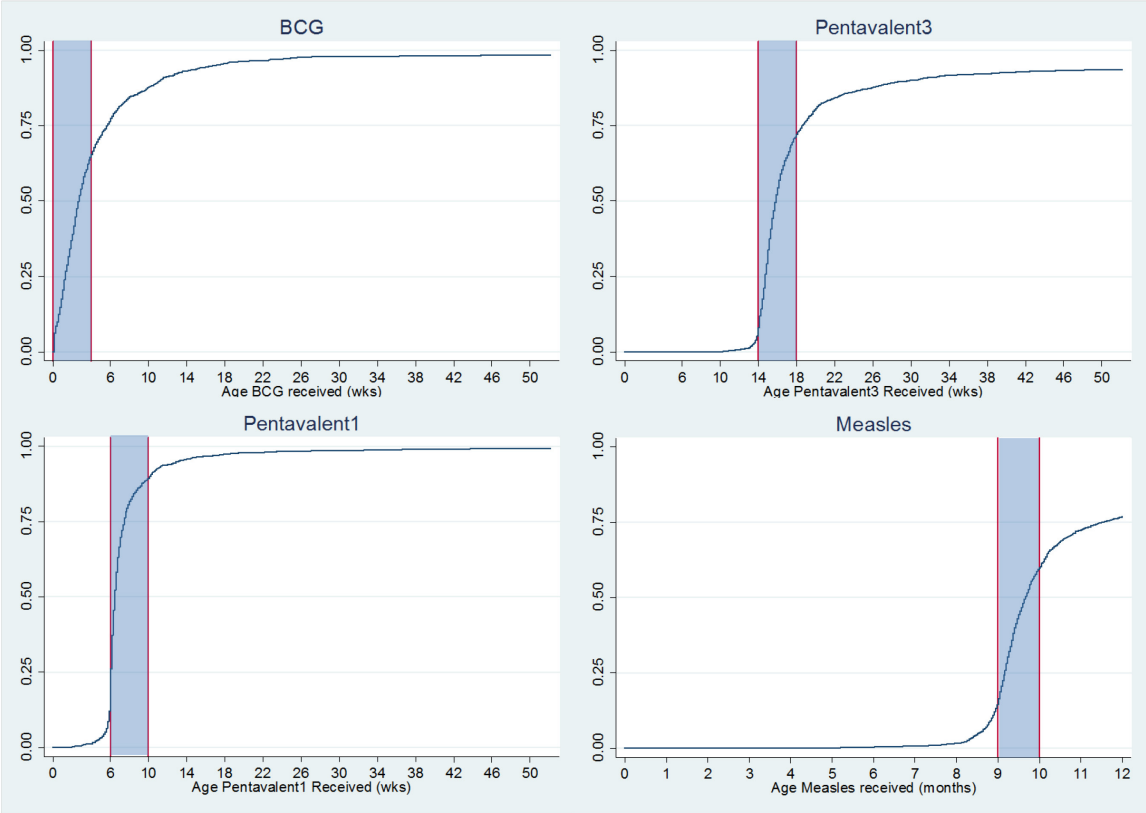
Abbreviation: RR, risk ratio

[1] Socioeconomic status derived from Principal Components Analysis of household possessions

Bold estimates and confidence intervals represent significant finding at an alpha of 0.05

4.7 Figures for Chapter 4

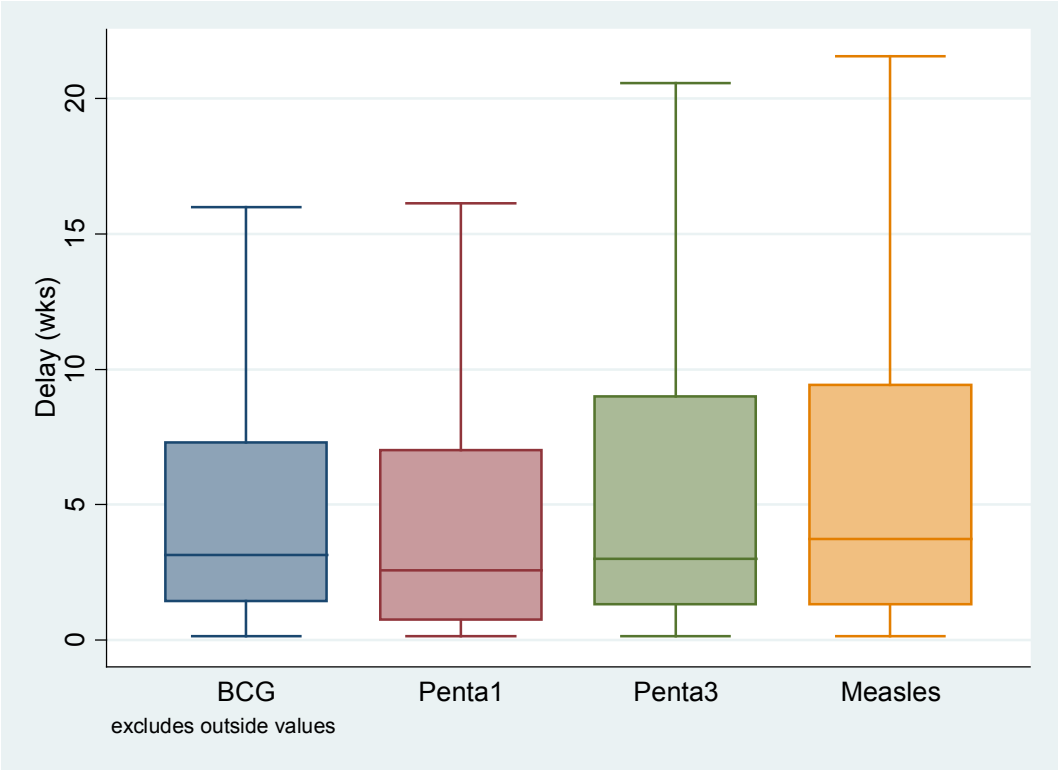
Figure 4.1 Inverse Kaplan-Meir curves for immunization timeliness by antigen in infants aged 12-23 months in Gem District, Kenya.



Abbreviations: BCG, Bacillus Calmette–Guérin vaccine; Pentavalent1, first dose of pentavalent vaccine; Pentavalent3, third dose of pentavalent vaccine

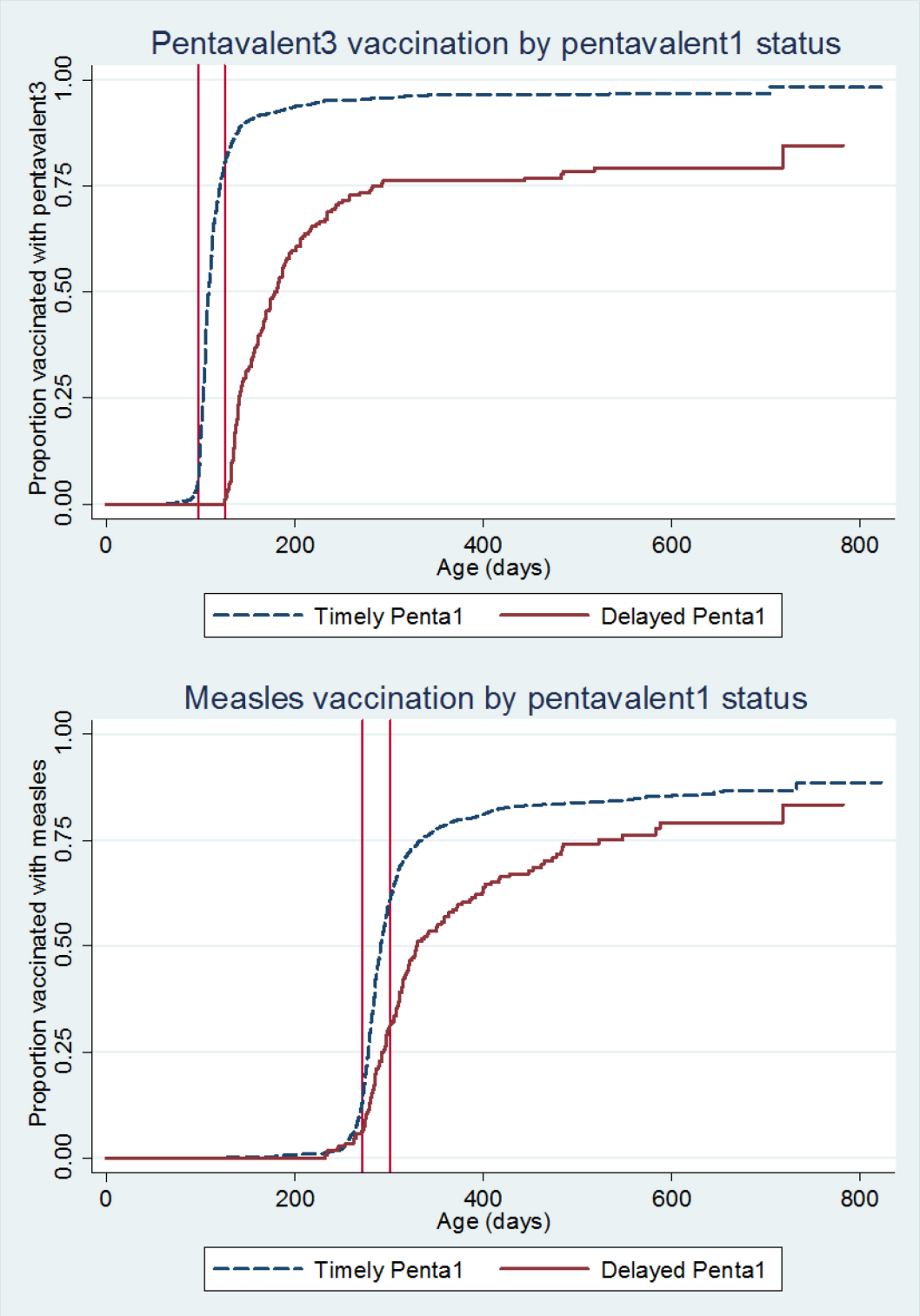
CAPTION: Shaded bars indicate timely window of vaccination. Infants censored at 12 months of age

Figure 4.2 Box plots for weeks delayed by antigen in infants aged 12-23 months in Gem District, Kenya



Abbreviations: BCG, Bacillus Calmette–Guérin vaccine; Pentavalent1, first dose of pentavalent vaccine; Pentavalent3, third dose of pentavalent vaccine

Figure 4.3 Inverse Kaplan-Meir curves for time to pentavalent3 and measles vaccination by pentavalent1 status



Vertical bars indicate the one month period vaccines were considered on time

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Chapter 5. Mobile-health interventions to improve immunization: Formative research findings and epidemiology of mobile phone ownership and short message system (SMS) behavior in rural western Kenyan women

5.1 Abstract

Objectives: To assess the feasibility, challenges, and willingness to receive mHealth interventions targeting pediatric immunization in rural western Kenya

Methods: Focus group discussions were conducted with 30 rural Kenyan mothers to inform an intervention trial using short message system (SMS) reminders and mobile money based incentives. A cross-sectional survey of 2393 mothers with infants aged 12-23 months was conducted to assess mobile phone ownership and SMS utilization. Predictors of phone ownership and SMS behavior were determined using multivariate logistic regression analyses.

Results: Overall, focus group participants thought mobile-health interventions could improve immunization coverage. Mothers mentioned several challenges to such interventions, including low mobile phone ownership, language barriers, and appropriate content. The wording of incentives to potential recipients was important as incentives were viewed as travel subsidies. From the cross-sectional survey, 55% of mothers owned a mobile phone, 76% received SMS, and 54% sent SMS in the past week. Significant predictors of mobile phone ownership included older maternal age, higher maternal literacy, increased maternal education, smaller households, and higher socioeconomic status. Maternal literacy, education, and phone ownership predicted receiving SMS. Marital status, socioeconomic status, and phone ownership predicted sending SMS.

Conclusions: Most mothers in rural Kenya had access to mobile phones and had received SMS previously, indicating the potential for mobile Health-based interventions to

improve immunization. Challenges to such interventions include unequal access to mobile phones and proper framing of the SMS reminders. mHealth interventions and programs are often implemented prior to soliciting community input. Despite the global increase in mobile phone ownership, additional efforts and consideration are needed to ensure the successful delivery and receipt of mHealth interventions to populations with low mobile phone ownership, but high levels of mobile phone access.

5.2 Introduction

For public health practitioners, vaccines remain one of the greatest tools at reducing childhood mortality and morbidity.[1] Current immunization programs are estimated to save over 2.5 million lives per year.[1] Despite their lifesaving potential, approximately 20% of children, or about 24 million infants, did not receive all the scheduled vaccines[1] and if they were vaccinated, they often received the vaccinations late.[2]

Traditionally, supply side strategies, such as improving cold chain capacity and increasing procurement, have been employed to address immunization coverage deficiences[3, 4], yet immunization gaps persist. Complimentary approaches to supply side strategies are demand-side interventions that target high transport costs, misperceptions and fear of vaccines, and forgetfulness of child's immunization. Two of these potential demand side interventions are reminder messages and small monetary incentives conditioned on vaccine receipt.

Incentives are a remunerable good or cash that is provided and conditioned on a participant's behavior. In the context of immunization, incentives could be given if a caretaker brings her child for timely immunization. Quantitative and qualitative research on pairing incentives and immunization is limited, yet the findings afford much promise. Studies conducted in Pakistan and India found that providing food vouchers or food provisions conditioned on vaccine receipt markedly improved vaccination coverage.[5, 6]

In addition to incentives, a reminder aimed at targeting parent's forgetfulness of their child's immunization appointments is another potential demand-based intervention. In high income countries, medical practitioners are recommended to send reminders for pediatric vaccines based on the strong evidence supporting reminders to improve

vaccination.[7, 8] Postal, electronic-mail, and voice mails may work well in higher income countries, but access to such commodities in lower income countries may hinder their implementation. With global increases in mobile phone ownership and access, particularly within lower-income countries[9], reminder messages delivered through SMS may also prove effective at improving vaccination rates.

Short message system (SMS) reminders, or text messages, modestly improved vaccination uptake in trials conducted in the United States.[10-13] Although the efficacy of SMS reminders on vaccination uptake has not been studied in resource-constrained settings, aside from a small pilot study[14], the majority of randomized controlled trials in sub Saharan Africa have found SMS reminders improve various forms of healthcare utilization.[15-23]

In the pilot study referenced above, 72 Kenyan mothers were randomized to receive SMS reminders and either $2 USD in mobile money or airtime. Although no control group was employed, 57% of the 72 infants received Pentavalent1 and Pentavalent2 on the scheduled dates while 88% of infants were vaccinated within three days of the scheduled date.[14] Of the 54 mothers who completed a follow-up visit, all participants reported that incentives and reminders would influence other mothers to get their child vaccinated on time.

The use of SMS reminders to improve a particular form of healthcare utilization is contingent on the targeted population's access or ownership of a mobile phone. In a 2009 national analysis of Kenyan mobile phone ownership, the authors found that despite 45% of the population owning a mobile phone, 85% of Kenyans had access to one and that the

strongest predictor of mobile phone ownership was higher education[24]. However, this analysis examined determinants of ownership in both sexes, and research shows a high gender gap in mobile phone ownership levels.[25]

A more recent analysis of adult patients and caregivers of sick children at Kenyan health facilities found that 60.5% of caregivers owned a mobile phone[26]. Similar analyses of mobile phone ownership determinants were conducted as above, with male gender, higher education, lower poverty, higher literacy, and urbanization being predictive of phone ownership. In a separate analysis of SMS use, education, age, and literacy were found to be statistically significant.[26] Importantly, in both analyses[24, 26], interaction terms with gender were not included.

In preparation for the Mobile Solutions for Immunization (M-SIMU) village randomized controlled trial that uses SMS reminders with or without small monetary incentives to improve vaccine coverage and timeliness in western Kenya, we conducted focus group discussions to receive local and contextual-specific feedback on the content and timing of the SMS reminders, incentive amounts, willingness to receive reminders and incentives, and address any problems or complications associated with delivering SMS reminders and incentives. Additionally, a baseline survey of the study area sought to examine the distribution of mobile phone ownership and SMS behaviors.

5.3 Methods

5.3.1 Focus Group Sample

The primary purpose of the focus group discussions was to inform the M-SIMU trial on SMS content and incentives. The Kenya Medical Research Institute (KEMRI) Demographic Surveillance System (DSS) database was searched to identify mothers with

children ages 12-23 months and residing in one of ten villages surrounding Siaya Town. From this list of eligible participants, a random sample of 48 mothers was taken (nine villages contributed five eligible participants and one village three participants). KEMRI/CDC staff approached eligible participants for informed consent to one of three focus group discussions (FGD). While taking informed consent, mothers were informed that a SMS password, written in the local language Dholuo, would be sent 1 day before the Focus Group to the phone number that they indicate having access to. The SMS passwords were unique for each individual and were grouped into colors, animals, and means of transportation. Mothers were reimbursed approximately $3.50 USD for round-trip transportation to the venue. The focus groups were led by a moderator and three assistants and conducted on June 3rd and 4th, 2013. Each focus group lasted approximately 2-2.5 hours and was conducted in the local language, Dholuo.

5.3.2 **Focus Group Data Collection**

5.3.2.1 **Individual questionnaires**

Prior to the start of the group discussion, individual questionnaires were conducted with each mother to collect demographic information, mobile phone ownership and characteristics, evaluate the ability to open and read an SMS message, assess whether the SMS password was received, and to rank-order the top 3 of 12 phrases that could be included on an SMS to encourage a mother to vaccinate her child. For ability to open and read an SMS message, KEMRI interviewers sent an SMS to the participant containing the question, "Hi, how are you today?" The interviewer observed the participant as she opened the message, read it, and answered the question. The response was coded as 'Yes, easily', if there was no delay in locating the SMS inbox and

opening the message. If the mother could not immediately locate the SMS inbox and open the message, the response was coded as 'Yes, with difficulty". If the mother could not open the message, or could not read, the response was coded as "No, cannot open or read".

5.3.2.2 **Focus group discussion**

A semi-structured questionnaire guide was used to elicit mother's responses on barriers to immunization, SMS reminders for pediatric immunization dates, and monetary incentives to motivate mothers to bring children for immunization (Appendix 3). The moderator was encouraged to probe further for interesting responses. For questions requiring individual responses within the group session, participants ranked the responses by either writing the answer on a small piece of paper or placing a pre-printed response in bins labeled #1 (i.e. favorite, preferred, best), #2 (i.e. second favorite, preferred, best), etc. These responses were made before any group discussion and were considered as independent, rather than group, responses. The six highest ranking phrases identified from the individual questionnaire were re-ranked privately during the focus group discussion.

In discussion about incentive amounts for immunization, participants were presented a scenario where a mother was too busy to bring her child for immunization and asked if providing small monetary incentive might cause this mother to bring her infant to the immunization clinic. The amounts ranged from 10-200ksh and were presented randomly one at a time. Participants placed a check mark next to the incentive amount if they thought it was sufficient enough to cause a mother to bring her infant for immunization.

Focus group discussions were audio recorded, transcribed in Dholuo, and then translated into English. Audio recordings were destroyed after transcription and translation. Mothers were given participant IDs, which were used to identify women during the focus group discussions. No names were recorded during discussions or written on questionnaires.

Responses in individual surveys and group settings were entered into Microsoft Excel and tabulated for frequencies, but no hypothesis tests were made. Results of focus group were resented thematically.

The protocol and informed consent for the Focus Group were approved by the Ethical Review Committee of KEMRI.

5.3.3 **Mobile phone ownership and SMS behavior Survey**

In March and April of 2013, KEMRI/CDC staff surveyed all known mothers with infants aged 12-23 months old from DSS-consented compounds in 120 villages of Gem District, Nyanza Province. The primary purpose of this survey was to collect demographic variables and immunization coverage to inform sample size and randomization for the M-SIMU village randomized controlled trial.

5.3.3.1 **Data Management and Analysis**

Trained KEMRI/CDC staff conducted surveys on Huawei Y200 smart mobile phones equipped with the ODK Collect application and preprogrammed with range limits and double data entry. Incoming data were cleaned as collected and community interviewers made follow-up visits for participants with ambiguous data. Analyses were performed using STATA/IC, version 11.2 (Stata Corp, College Station, Texas).

The primary outcomes were proportions of self-reported mobile phone ownership, receiving SMS, and sending SMS. Mobile phone ownership was coded as '1' if the mother is the primary owner of a mobile phone and '0' if the mother either shared or did not own a mobile phone. In addition, participants who did not own a mobile phone were asked if they had access at the household or compound. For receiving and sending SMS, participants were asked if they regularly received or sent SMS reminders, coded as '1'. For those that indicated receiving reminders, participants were asked how soon SMS were received if a mother owns the mobile phone or how quickly SMS were relayed if mobile phone is shared. In addition, mothers were queried on the frequency of sending and receiving SMS in the last week.

In addition to primary outcome variables, participant's self-reported demographic variables, which were included in regression analyses. These variables included number of children under 5 years old that slept in the house last night, the number of people regularly in the household, marital status, socioeconomic status, and maternal age, highest level of education attempted, and ability to read English. Data collected as continuous variables were categorized based on reporting relevance and interpretability. Maternal age was categorized into mothers aged 15-24 years, 25-34 years, and greater than 34 years. Maternal education was grouped into categories 0 to 8, 9 to 12, and greater than 12 years of education attempted. Number of children under five years in the household was categorized as 1, 2 or 3 number of children. The socioeconomic variable was calculated by KEMRI/CDC staff using principal components analysis from variables on the KEMRI/CDC DSS Household Socio-economic Form. These variables included occupation, drinking water treatment, type of cooking fuel, and possessions. The socio-

economic status was provided in quintiles and collapsed to lower 40% and upper 60% for present analysis.

Prior to construction of regression models, data were checked for completeness and accuracy. Frequency distributions were performed to explore data. Unadjusted logistic analyses were conducted with the three primary outcomes: mobile phone ownership, receiving SMS, and sending SMS for each demographic variable. For each primary outcome's adjusted model, variables were selected using forward step wise Akaike Information Criteria to obtain adjusted odds ratios and 95% confidence intervals. An alpha of 0.05 was used for all hypothesis testing.

5.4 Results

5.4.1 Focus Groups

Forty-eight mothers with children ages 12-23 months were eligible for enrollment. Of these 48 mothers, 33 women consented to the study, eight were not at home when staff visited, six women refused participation, and one was not contacted. Three consented women did not attend the FGD. The following results are for the 30 women who consented and participated in the FGDs.

5.4.1.1 Maternal demographics and mobile phone ownership/literacy:

The majority of the mothers participating in the FGD were ages 20-24 years old, had some primary level education and were evenly distributed in the number of previous pregnancies (Table 5.1). Mobile phone literacy and characteristics of mother's mobile phone are presented in Table 5.2. Twenty-eight mothers (93%) owned a mobile phone and 90% of mothers brought the mobile phone with them to the FGD. For those that brought a mobile phone to the FGD, one-third of participants had less than 1 Kenyan

Schilling (KSH) of airtime on the phone and 41% had 1-5ksh (85ksh=$1.00 USD as of October 2014). Approximately one-fourth of mobile phones had a battery charge of 76-100%, while 22% had less than 25% charge. Two-thirds of mothers were able to recall the password from the SMS sent one day prior to the FGD. When sent an SMS during the individual questionnaire, 90% of mothers were easily able to open and read the message.

The first FGD was conducted with 12 participants from 6 villages. The second and third FGD were each conducted with 9 participants from 6 villages, respectively. Overall, the sample spanned 10 different villages.

5.4.1.2 **Barriers to immunization coverage:**

Mothers were asked to discuss perceived barriers in bringing their child for immunization. Bus fare, long distance, lack of information, ignorance and the belief that clinics may be out of vaccine were common reasons that mothers indicated as barriers to immunization coverage.

Long distance to the clinic and its associated travel costs were common explanations.

> *Sometimes distance also becomes an issue but when I do not have bus fare can make me feel discouraged.* Group 3-Participant 3

But mothers also believe the effect of distance could be overcome if the importance of immunization was understood.

> *What I can say about distance is that it depends on a person's conviction. Sometimes it can be far but when you consider the importance of vaccinating a baby, you just make efforts of going.* Group 3-Participant 5

Another commonly discussed barrier was ignorance in regards to vaccine's effectiveness.

> *Me, I want to say that first it is illiteracy or ignorance. This means that somebody assumes, or she is a person of the past or she did not go to school. So she will say that even them their parents did not go to school and they were not taken for vaccines and yet we exist and do not fall sick often. Today's children are taken for vaccines and yet they still fall sick.* Group 3-Participant 2

> *....even in the past children survived without vaccines, so she doesn't see the need to take her child for vaccination.* Group 2- Participant 3

Barriers to timely immunization: The moderator explained timeliness of vaccination in relation to the EPI schedule and asked participants if these barriers were dissimilar to the barriers for immunization coverage. Caregiver's forgetfulness was a common barrier identified in all three focus groups.

> *Some people forget, she stays until one day she hears that somebody is taking her child to clinic. That is when she remembers that she was supposed to take her child to clinic. Secondly, she does not know how to read the date which was written on the clinic card.* Group 3-Participant 2

Some mothers may be reluctant to bring their child for immunization which hints at the potential of either incentives or reminders to 'nudge' mothers into bringing the child for vaccination earlier.

> *Those who take their children late means somebody is just taking the child for what to do but she is not fully for the idea.* Group 3, Participant 8

And as seen with barriers to bringing children for any immunization, far distances to the clinic and unavailability of vaccines were identified as reasons for delayed immunization.

> *....perhaps she got the message early but she is coming from a far place so she tried to look for transport money but did not find in time."* Group 2-Participant 1
>
> *"Some people take them late because sometimes she takes a child in time but she is told that the vaccine is not available and so she should come back another time and perhaps that time the recommended time shall have passed.* Group 2-Participant 2

However, mothers remained optimistic and provided solutions to address timely immunization deficiencies.

> *But how I perceive it, I think that when a person delivers at the health facility or when mothers are going to clinic when expecting, they usually take phone numbers. If only they can use those phone numbers to remind somebody then they can be of help because there are some who do not know dates. Surely, they totally do not know and some also assume. Therefore, if they can use the phone numbers to remind mothers it can be of great help.* Group 3- Participant 2

5.4.1.3 **Components and timing of an SMS reminder message:**

Participants were informed that an SMS could serve as a reminder to immunize their child. We then queried mothers on what components of an SMS reminder are essential to ensure the SMS prompts the mother to bring her child for vaccination. Date of vaccination, location, child's name, and the specific vaccine being reminded were components expressed in all three FGDs. Some mothers suggested that the SMS reminder should stress the importance of vaccination.

> *Other than the meaning of vaccination, we request that you include the importance of the vaccine…that is what can make the mother take her child to the clinic.* Group 2- Participant 1

When asked about the timing of delivery of SMS reminders, 63% of participants reported that they would prefer reminders sent 2-3 days before the scheduled vaccination, while 23% preferred reminders sent the day before.

> *2-3 days is good because it allows for one to prepare early, so when the day comes one is ready such that if she was far away* Group 1- Participant 11

No participants thought that the reminder should be sent on the day of vaccination

> *When that [SMS] is sent on the same day [with the vaccine date] and sometimes on that day you do not have a phone within reach. So you cannot read the SMS….Sometimes you are on a journey or something is holding you. You can be sent the SMS but there is no way you can make it, therefore at least a day before is better.* Group 1-Participant 2

5.4.1.4 **Phrases and sayings in an SMS to motivate mothers to vaccinate their child:**

The 12 phrases were compiled by asking KEMRI/CDC staff for common phrases in the local language and any other phrase that may prompt a mother to attend the immunization clinic. The phrases were classified into 5 different categories; motivational (n=5), informational (n=2), religious (n=1), humorous (n=1) and local sayings (n=3), (Table 5.3).

The results of mother's individual rankings of phrases that could be attached at the end of an SMS reminder are presented in Table 5.4. Phrase #1, "Vaccinations save the lives of Kenyan babies", had the highest ranked weighted score (61 points), followed by Phrase #2, "Baby Thomas <personalized> is happy when healthy" (29 points), and

Phrase #3, “Most mothers in your area are getting their child vaccinated. Be one of them!” (26 points). The preferred order was identical to the individual rankings (Table 5.5).

Overall, the participants preferred informational or motivational types of messages as compared to humorous or local sayings and proverbs.

> *Me, I feel those proverbs or wise sayings cannot help because they can be sent but I do not understand. So I think we should go directly to the information* Group 1- Participant 3

And in regards to the most preferred phrase, “Vaccinations save the lives of Kenyan babies”.

> *I chose it because when children get vaccinated, all of them it is good because sometimes yours gets vaccinated and another does not get vaccinated. If polio attacks the one not yet vaccinated you know yours can also contract polio.* Group 3- Participant 6

> *I think it can be good because what is written here already makes the mother feel happy such if you add on to the message she can be happier and be anxious to take her child for vaccination* Group 1- Participant 6

5.4.1.5 **Incentives for immunization**

Twenty-seven percent of mothers said that 100 KSH, the first amount presented to the group, would motivate the mother to vaccinate her child. A dose-response with increasing incentive amount and the mother bringing her child for vaccination was observed with the effect plateauing at 175 KSH where 90% of mothers indicated this incentive amount would be sufficient to motivate the mother to bring her infant for vaccination (Figure 5.1). Fifty KSH (0.60 USD) was the smallest amount that participants thought would motivate the mother in the scenario.

When participants were asked to describe why they picked incentive amounts, in all three focus groups, the conversation centered on transportation costs.

> *I think as so long as a person is given an amount which is enough for transport it is ok. So, even if you are given 50 KSH for fare, you are going to save life of your child.* Group 2- Participant 9

> *I come from Karapul and I want a motorcycle to take to clinic at a District hospital. The motorcycle rider will take 50 KSH such that I will remain with nothing meaning I will walk back on foot.* Group 3- Participant 3

> *200 KSH is good because sometimes, let us say the day for Thomas's mother to go to clinic has come and maybe she had a job she needed to do because she does not have money. Now, if she was to be given 10 KSH, she will say let it be but if it is 200 KSH she can prioritize going to clinic because she is sure of getting that money.* Group 1- Participant 3

Some mothers expressed concern that giving too small of an incentive would be insulting.

> *Thomas mother will wonder how much you despise her. That is despising because you have come from far and have spent even 100 KSH and you want to go back with 100 KSH and then somebody wants to give 50 KSH, I think he/she should just leave.* Group 3- Participant 2

Lastly, there were a few people who thought any incentive amount would be appropriate as bringing your child for vaccination is a good thing to do.

> *I think whoever understands importance of vaccination should not despise amount that she is given because a child must be taken for vaccination and should appreciate amount that she is given*. Group 2- Participant 3

5.4.1.6 **Anticipated Challenges**

Several challenges were identified across the three focus groups. First, mothers expressed concern that messages would not be relayed to those who share a mobile phone. Second, illiterate mothers would have difficulty benefitting from the intervention.

Instead, participants suggested calling mothers when vaccinations are due. In two of the groups, mothers recommended including who the SMS was being sent by, as mobile operators tend to send many unwanted SMS.

> *I cannot trust it because I do not know where it has come from and how it started. Nowadays messages are sent aimlessly to phones. You switch on your phone and find a message that you do not know its origin.* Group 3- Participant 9

Other challenges recognized were mobile phones not being adequately charged, the need for different languages, complex language, and sending an SMS to mothers who do not want to receive them.

5.4.2 **Mobile Phone Ownership and SMS Utilization Survey**

5.4.2.1 **Mobile Phone Ownership analyses**

Mobile phone ownership and SMS utilization data were collected from, 2393 and 452 mothers with infants aged 12-23 months old respectively. Demographic variables were missing for 44 participants. In a final sample of 2359 participants, 55% (n=1301) of mothers self-reported owning a mobile phone while 33.7% (n=794) and 4.9% (n=117) had access at the household and compound (Table 5.6). Mothers that reported no ownership or access to a mobile phone was 6.2% (n=147).

The results of bivariate logistic regression analyses for mobile phone ownership, as compared to not owning a mobile phone, are presented in Table 5.7. Older mothers, ability to read English language, higher maternal education, and socioeconomic status were significant predictors of owning a mobile phone, as compared to not owning a mobile phone. Marital status, the number of children under five years old sleeping in the

household, and the size of the household were not significantly associated with the outcome

In multivariate analysis, women aged 25 to 34 years (OR: 1.59; 95%CI 1.32-1.91) and women greater than 35 years old (OR: 1.90; 95%CI 1.40-2.58) were more likely to own a mobile phone than women aged 15 to 24 years. Mothers with education greater than 12 years, (OR: 2.77; 95%CI 1.73-4.42), were more likely to own a mobile phone than mothers with less than eight years of education. Mothers who were in the upper 60% of socioeconomic status (OR: 1.80; 95%CI 1.52-2.14) were significantly associated with mobile phone ownership as compared to those in the lower 40%. Both the inability and difficulty with reading English language was associated with not owning a mobile phone, (OR: 0.33; 95%CI 0.24-0.48) and (OR: 0.65; 95%CI 0.54-0.79), respectively. Mothers in the largest households were also significantly associated with not owning a mobile phone as compared to mothers living in smaller households, (OR: 0.78; 95%CI 0.61-0.99).

5.4.2.2 **Receiving SMS analyses**

Of the 452 mothers with SMS utilization data, 76.1% reported regularly receiving SMS. When stratified by phone ownership, 96.1% of those owning a mobile phone receive SMS compared to 49.7% who do not own a phone, $p<0.0001$ (Table 5.8). Approximately 97% of mothers received an SMS either immediately or within 1 day of it being received, if relayed.

Bivariate analyses found that the mother's ability to read English, higher maternal education, smaller household sizes, higher socioeconomic status, and mobile phone ownership were significantly associated with receiving SMS (Table 5.9). In multivariate logistic regression analyses for predictors of receiving SMS versus not receiving SMS,

only higher socioeconomic status (OR: 1.79; 95%CI 1.01-3.19), monogamous marriage (OR: 2.47; 95%CI 1.13-5.44) and mobile phone ownership (OR: 27.9; 95%CI 13.1-59.5) were associated with receiving SMS (Table 5.9). Analyses with mobile phone ownership excluded from the multivariate model found that English literacy, maternal education, and high socioeconomic status were predictive of receiving SMS (Table 5.10).

5.4.2.3 **Sending SMS analyses**

Approximately 53.5% of the 452 mothers reported regularly sending SMS. Similar to receiving SMS, the proportion of mothers that sent SMS was higher in those who own a mobile phone (68.5%) as compared to those who do not own a mobile phone (37.4%, Table 5.8).

Bivariate analyses of predictors of sending SMS reveal that ability to read English language, higher maternal education, smaller number of children under five years old in household, higher socioeconomic status, and phone ownership were significantly associated with the outcome (Table 5.11).

In multivariate logistic regression analyses for predictors of sending SMS, mothers inability to read English (OR: 0.26; 95% CI 0.08-0.82) as compared to the control, was associated with not sending SMS. Mothers who completed 12 or more years of school (OR: 3.24; 95%CI 1.12-9.38), as compared to those who attempted less than eight years and mothers who owned a mobile phone ownership (OR: 2.78; 95%CI 1.86-4.15), as compared to those who do not, were both associated with sending SMS (Table 5.11). When mobile phone ownership was excluded from the multivariate model, English literacy and maternal education were predictive of sending SMS (Table 5.12).

5.5 Discussion

In order to ensure that SMS reminders, and mHealth interventions as a whole, are successful, qualitative research prior to implementation is critical to account for local context. A range of qualitative studies within the United States has generally found that parental opinions of vaccination appointment SMS reminders to be accepted effective.[27-32] However, there is a paucity in research from lower income countries, with only two studies from Burkina Faso and Nigeria reporting on acceptance of SMS reminders for vaccination[33, 34] and several other studies reporting on SMS acceptance for tuberculosis[35, 36], malaria[37, 38], and HIV treatment.[39, 40] This study attempts to address some of these gaps in qualitative literature surrounding mHealth interventions for immunization in lower income countries.

In rural western Kenya, our focus group found that 77% of mothers thought providing 100KES and SMS reminders would be very helpful at encouraging mothers to bring their child for vaccination (Figure 5.2). Previous studies from Burkina Faso and Nigeria report that, respectively, 100% (of n=142) and 77% (of n=399) of mothers would be willing to receive an SMS to remind them of their child's immunization appointment.[33, 34] Although we did not quantify whether focus group mothers would like to receive SMS, the proportion of mothers that believe SMS and incentive to be effective at getting infants vaccinated may serve as a proxy. However, the participants indicated that high levels of mobile phone sharing, phones not routinely charged, language barriers, and not knowing the source of the SMS as potential challenges to implementing SMS-based interventions. To counteract low levels of mobile phone ownership, 55% in our baseline survey, SMS reminders could be personalized to ensure that the message is

correctly relayed. Additionally, intended recipients should alert the mobile phone owner that reminders will be sent. Our baseline data indicates that 50% of mobile phone sharers receive SMS suggesting that reminder programs or interventions may be feasible in areas with low mobile phone ownership.

To address the issue of language barriers, but not literacy, the language of the recipient should be determined for targeted SMSs to that person. Moreover, SMS reminders should be constructed using simple, concise wording and indicating who is sending the SMS. Still there are some barriers that cannot be controlled for, such as uncharged mobile phones and people's willingness to relay reminders and incentives. Lastly, caution should be taken if implementing a two-way SMS intervention. In our study sample, the majority of mothers did not have enough airtime to send one SMS. If a program or intervention requires participant feedback, providing toll-free communication lines or airtime may be needed.

We explored the use of additional phrases to attach at the end of an SMS reminder because of quantitative [15] and qualitative work[37] demonstrating that motivationally worded SMS reminders may increase the likelihood that messages are read. Two of the top three preferred choices directly pertained to vaccination while the other was personalized and more broadly spoke about the child's health. These three additional phrases plus a phrase commenting on the vaccines availability will be included in SMS reminders used in the M-SIMU trial and will be randomized by dose to potentially determine, although underpowered, if any of these additional phrases were more effective at yielding timely immunization.

The timing of SMS reminder delivery is also important. As revealed in the focus group, SMS reminders are preferred to be received before the date of vaccination. Broadly, sending reminders too early (i.e. day of scheduled vaccination) may not produce the desired behavior change because mothers may have planned commitments or, more likely in areas with low mobile phone ownership, not enough time is given for the reminder to be relayed to the intended recipient. Previous qualitative work found that 60% of Nigerian mothers prefer an SMS reminder sent one day before immunization visit and only 3% prefer the reminder on the same day as vaccination.[33] Equally important, and mentioned in the focus group, is sending the reminder message too early as mothers may forget the reminder message.

In regards to incentives, FGD mothers interpreted an immunization incentive as a transportation reimbursement. Providing incentives specific to an individual's transport cost is problematic for research trials and scaled programs. To not disappoint, or even negatively influence the decision of, those whose transport costs are greater than the incentive, the incentive could be described as a reward for taking care of the child's health.

Our findings that older, more educated, literate, wealthier women were more likely to own a mobile phone is not surprising when compared to other estimates in Kenya[24, 26] and globally.[41] Historically, these predictors of mobile phone ownership are often similar to predictors of healthcare utilization. Less educated, younger, impoverished women are individuals that would most likely benefit from mHealth interventions such as reminders and mobile-money based incentives, yet low levels of phone ownership complicates the delivery and receipt of intervention. Somewhat

promising is that, despite low levels of ownership, 94% of mothers in our baseline survey indicated that they had access to a mobile phone at the compound level. It is likely that the proportion with access is even higher as we did not ask about neighbors. Still, this potential weakness needs to be acknowledged and addressed in future mHealth interventions.

Our study had several limitations. In regards to the focus group discussions, the largely positive findings may be a result of 'courtesy bias' in that the participants provided answers that they thought might please the moderator and research team. To minimize this, the M-SIMU randomized controlled was only mentioned after the conclusion of focus groups. Still, the participants knew that KEMRI/CDC was hosting the focus group and there is high population knowledge about KEMRI/CDC's research agenda. Pertaining to the mobile phone ownership and SMS behavior survey, we attempted to survey all caregivers with children 12-23 months of age. To facilitate this, KEMRI/CDC provided us a census. The provided census may have contained missing households as surveillance activities in Gem District recently resumed and the mapping of households may not be complete. It is possible that these missing households are in remote locations which one would assume to have lower socioeconomic status. Therefore, it is possible that we have overestimated mobile phone ownership. Additionally, due to a supervisory oversight, the small sample size for SMS utilization prevents drawing strong conclusions about predictors of sending and receiving SMS. As part of the larger Mobile Solutions for Immunizations (M-SIMU) trial, SMS utilization analyses will be revisited with a sample size of over 2000 mothers.

In conclusion, there is little formative research on willingness to receive, content of, and delivery timing of SMS reminders in resource-limited settings. The optimization of these features, while also accounting for high levels of mobile phone sharing and phone ownership concentrated in wealthier more educated women, prior to project implementation will likely increase the probability of enacting positive behavior change.

5.6 Tables for Chapter 5

Table 5.1 Demographics of Focus Group Discussion mothers with infant aged 12-23 months in Siaya District, Kenya, 2013.

Characteristic	N (%)
Maternal Age (years)	
20-24	16 (53%)
25-29	8 (27%)
30-37	6 (20%)
Maternal Education (Highest level attempted)	
None	2 (7%)
Primary	14 (47%)
Secondary	8 (27%)
Post-secondary	6 (20%)
Number of previous pregnancies	
0	10 (33%)
1	6 (20%)
2	4 (13%)
3-9	10 (33%)

Table 5.2 Mobile phone ownership and characteristics of Focus Group Discussion mothers with infant aged 12-23 Months in Siaya District, Kenya, 2013.

Mobile Phone Access	**N (%)**
Own	28 (93%)
Household	1 (3%)
Compound	1 (3%)
Phone brought to FGD	
Yes	27 (90%)
No	3 (10%)
Credit Amount on Phone (KSH)[1,2]	
0-0.99	9 (33%)
1-5	11 (40%)
5-20	7 (26%)
Battery Charge on Phone (%)[1,3]	
0-25	6 (22%)
26-50	1 (4%)
51-75	7 (26%)
76-100	13 (48%)
Remember password sent 1 day before FGD	
Sent to wrong number	1 (3%)
No	9 (30%)
Yes	20 (67%)
Can open and read SMS	
No, can't open or read	2 (7%)
Yes, with difficulty	1 (3%)
Yes, easily	27 (90%)

Abbreviations: FGD, focus group discussion; KSH, Kenyan Schilling; SMS, short message system

[1] Only asked of mothers who brought phone to focus group (N=27)
[2] 85 KSH= 1 USD as of October 2014
[3] Percent of a fully charged (100%) phone

Table 5.3 Phrases to be attached at the end of an short message system (SMS) reminder to prompt mothers to vaccinate their child

#	**Phrase**	**Category**
1.	Vaccinations save the lives of Kenyan babies.	Informational
2.	Baby Thomas is happy when healthy	Motivational
3.	It takes a village to raise a child	Motivational
4.	Hope resides in Togetherness	Motivational
5.	Do not respond to a mosquito with a hammer. You will hurt yourself	Humorous
6.	When a ripe fruit sees an honest man, it drops	Motivational
7.	A joyful heart is good medicine, But a broken spirit dries up the bones- Philippians 4:6-7	Religious
8.	If you start early you won't have to see a magician	Local saying
9.	The brain makes the person	Local saying
10.	An antelope is not anyone's goat	Local saying
11.	Most mothers in your area are getting their children vaccinated, be one of them!	Motivational
12.	80% of children in this area get vaccinated	Informational

Table 5.4 Individually ranked mothers' preferences for phrases to be included at the end of a short message system (SMS) reminder for pediatric immunizations

#	Phrase	1st Choice	2nd Choice	3rd Choice	Weighted Score[1]
1.	Vaccinations save the lives of Kenyan babies	17 (57%)	3 (10%)	4 (14%)	61
2.	Baby Thomas is happy when healthy	5 (17%)	6 (20%)	2 (7%)	29
11.	Most mothers in your area are getting their child vaccinated, be one of them!	3 (10%)	6 (20%)	5 (17%)	26
3.	It takes a village to raise a child	2 (7%)	5 (17%)	2 (7%)	18
7.	A joyful heart is good medicine, but a broken spirit dries up the bones- Philippians 4:6-7	1 (3%)	3 (10%)	4 (14%)	13
12.	80% of children in this area get vaccinated	2 (7%)	1 (3%)	4 (14%)	12
8.	If you start early, you won't have to see a magician		5 (17%)	2 (7%)	12
5.	Do not respond to a mosquito with a hammer. You will hurt yourself		1 (3%)	1 (4%)	3
4.	Hope resides in togetherness			3 (10%)	3
9.	The brain makes the person			2 (7%)	2
6.	When a ripe fruit sees an honest man, it drops				0
10.	An antelope is not anyone's goat				0

[1] Weighted score is the sum of rankings whereby 3 points were given for 1st choice, 2 points given for second choice, and 1 point given for 3rd choice.

CAPTION: Responses were recorded during the individual survey prior to start of the Focus Group

Table 5.5 Group ranked mothers' preferences for phrases to be included at the end of a short message system (SMS) reminder for pediatric immunizations

#	Phrase	1st Choice	2nd Choice	3rd Choice	Weighted Score[1]
1.	#1 Vaccinations save the lives of Kenyan babies	14(47%)	6 (20%)	2 (7%)	56
2.	#2 Baby Thomas is happy when healthy	6 (20%)	6 (20%)	10 (33%)	40
11.	#11 Most mothers in your area are getting their child vaccinated, be one of them!	4 (13%)	7 (23%)	6 (20%)	32
8.	#8 If you start early, you won't have to see a magician	4 (13%)	2 (7%)	3 (10%)	19
7.	#7 A joyful heart is good medicine, but a broken spirit dries up the bones- Philippians 4:6-7	1 (3%)	3 (10%)	3 (10%)	12
3.	#3 It takes a village to raise a child	1 (3%)	3 (10%)	1 (3%)	10
12.	#12 80% of children in this area get vaccinated		2 (7%)	5 (17%)	9
4.	#4 Hope resides in togetherness		1 (3%)		2

[1] Weighted score is the sum of the rankings whereby 3 points were given for 1st choice, 2 points given for second choice, 1 point given for 3rd choice.

CAPTION: The top 6 phrases from the individual survey were used for each focus group discussion (FGD) and re-ranked in the group setting. Phrases #1, #2, #3, and #11 were discussed in each FGD. Phrases #7 and #8 were discussed in 2 groups. Phrase #12 discussed in 1 group

Table 5.6 Demographics of rural western Kenyan mothers with infant ages 12-23 months old in mobile phone ownership survey

Characteristic	N	%
Phone Ownership		
Owns	1301	55.2%
Access at household	794	33.7%
Access at compound	117	4.9%
None	147	6.2%
Maternal Age (years)		
15-24	1109	47.0%
25-34	1008	42.7%
>35	242	10.3%
Mother's ability to read English		
Easily	1308	55.4%
With Difficulty	870	36.9%
Not At All	181	7.7%
Maternal education (years)		
0-8	1282	54.4%
9-12	944	40.0%
>12	132	5.6%
Marital Status		
Single/Divorced/Widowed	381	16.1%
Monogamous Married/Cohabitating	1719	72.9%
Polygamous Married/ Cohabitating	259	11.0%
Number of children under 5 years old in household		
≤ 1	968	41.0%
2	1049	44.5%
≥ 3	342	14.5%
Number of persons in household		
≤ 3	617	26.2%
4-5	1139	48.3%
6-14	603	25.5%
Socioeconomic status quintile[1]		
Bottom 40%	943	40.0%
Upper 60%	1416	60.0%

[1]Socioeconomic status derived from Principal Components Analysis of household possessions

Table 5.7 Bivariate and multivariate analyses for predictors of mobile phone ownership in mothers with infants ages 12-23 months old

Characteristic	Phone Share		Own Phone		Unadjusted OR		Adjusted OR	
	N	%	N	%	OR (95%CI)	P value	OR (95%CI)	P value
Maternal age								
15-24 years	555	52.5%	554	42.6%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
25-34 years	408	38.6%	600	46.1%	1.47 (1.24-1.75)	<0.0001	1.59 (1.32-1.91)	<0.0001
>35 years	95	9.0%	147	11.3%	1.55 (1.17-2.06)	0.002	1.90 (1.40-2.58)	<0.0001
Mother reads English								
Easily	496	46.9%	812	62.4%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	442	41.8%	428	32.9%	0.59 (0.50-0.70)	<0.0001	0.65 (0.54-0.79)	<0.0001
Not At All	120	11.3%	61	4.7%	0.31 (0.22-0.43)	<0.0001	0.33 (0.24-0.48)	<0.0001
Maternal education								
0-8years	639	60.4%	644	49.5%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
9-12years	394	37.2%	550	42.3%	1.39 (1.17-1.64)	<0.0001	1.13 (0.94-1.36)	0.200
>12years	25	2.4%	107	8.2%	4.25 (2.71-6.65)	<0.0001	2.77 (1.73-4.42)	<0.0001
Marital status								
Single/Divorce	170	16.1%	211	16.2%	*Ref.*	*Ref.*		
Monogamous Married	773	73.0%	946	72.7%	0.99 (0.79-1.23)	0.902		
Polygamous Married	115	10.9%	144	11.1%	1.00 (0.73-1.38)	0.957		
Children < 5 years old in house								
≤1	421	39.8%	547	42.0%	*Ref.*	*Ref.*		
2	471	45.1%	572	44.0%	0.92 (0.77-1.10)	0.371		
≥3	160	15.1%	182	14.0%	0.88 (0.68-1.12)	0.292		
Persons in household								
≤3	270	25.5%	347	26.7%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
4-5	503	47.5%	636	48.9%	0.98 (0.81-1.20)	0.871	0.94 (0.76-1.16)	0.549
6-14	285	27.0%	318	24.4%	0.87 (0.69-1.09)	0.219	0.78 (0.61-0.99)	0.041
SES Quintile[1]								
Bottom 40%	515	48.7%	428	32.9%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Upper 60%	543	51.3%	873	67.1%	1.93 (1.64-2.29)	<0.0001	1.80 (1.52-2.14)	<0.0001

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; SES, socioeconomic status

[1] SES derived from Principal Components Analysis of household possessions

Table 5.8 Short Message System (SMS) utilization and frequency by mobile phone ownership

	Does not own phone	**Owns Phone**	**P value**
Receives SMS	97 (49.7%)	247 (96.1%)	P<0.0001
How soon SMS received			P=0.001
Immediately	60 (61.9%)	197 (79.8%)	
Within a day	30 (30.9%)	46 (18.6%)	
After 1 day	7 (7.2%)	4 (1.6%)	
Median SMS received per week	3	5	P=0.0534
Sends SMS	73 (37.4%)	169 (65.8%)	P<0.0001
Median SMS sent per week	3	3	p=0.486

Abbreviation: SMS, short message system

Table 5.9 Bivariate and multivariate analyses for predictors of receiving SMS in the past week in mothers with infants ages 12-23 months old

Characteristic	Don't Receive N %	Receive N %	Unadjusted OR OR (95%CI)	P value	Adjusted OR OR (95%CI)	P value
Maternal age						
15-24 years	52 58.2%	156 45.5%	*Ref.*	*Ref.*		
25-34 years	45 41.7%	150 43.7%	1.11 (0.70-1.75)	0.652		
>35 years	11 10.2%	37 10.8%	1.12 (0.53-2.36)	0.763		
Mother reads English						
Easily	52 48.6%	197 57.3%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	42 39.3%	136 39.5%	0.85 (0.54-1.35)	0.505	1.52 (0.83-2.78)	0.178
Not At All	13 12.2%	11 3.2%	0.22 (0.09-0.53)	0.001	0.48 (0.15-1.60)	0.234
Maternal education						
0-8years	67 65.1%	162 47.9%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
9-12years	34 33.0%	152 45.0%	1.85 (1.16-2.95)	0.010	1.63 (0.54-2.76)	0.113
>12years	2 1.9%	24 7.1%	4.96 (1.14-21.6)	0.033	6.70 (0.89-2.96)	0.089
Marital status						
Single/Divorce	23 21.3%	52 15.1%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Monogamous Married	78 72.2%	260 75.6%	1.47 (0.85-2.56)	0.168	2.47 (1.13-5.44)	0.024
Polygamous Married	7 6.5%	32 9.3%	2.02 (0.78-5.25)	0.148	3.33 (0.99-11.2)	0.051
Children < 5 years old in house						
≤1	44 41.1%	150 43.7%	*Ref.*	*Ref.*		
2	49 45.8%	131 38.2%	0.78 (0.49-1.25)	0.310		
≥3	14 13.1%	62 18.1%	1.30 (0.66-2.54)	0.444		
Persons in household						
≤3	22 20.6%	94 27.3%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
4-5	62 57.9%	152 44.2%	0.57 (0.33-0.99)	0.048	0.53 (0.26-1.07)	0.077
6-14	23 21.5%	98 28.5%	1.00 (0.52-1.91)	0.993	1.21 (0.54-2.76)	0.641
SES Quintile[1]						
Bottom 40%	57 53.8%	110 32.0%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Upper 60%	49 46.2%	234 68.0%	2.47 (1.59-3.86)	<0.0001	1.79 (1.01-3.19)	0.047
Phone Ownership						
Share	98 90.7%	97 28.2%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Own	10 9.3%	247 71.8%	25.0 (12.5-49.8)	<0.0001	27.9 (13.1-59.5)	<0.0001

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; SES, socioeconomic status

[1] SES derived from Principal Components Analysis of household possessions

Table 5.10 Bivariate and multivariate analyses for predictors of receiving SMS in the past week in mothers with infants ages 12-23 months old, excluding mobile phone ownership variable

Characteristic	Don't Receive		Receive		Unadjusted OR		Adjusted OR	
	N	%	N	%	OR (95%CI)	P value	OR (95%CI)	P value
Maternal age								
15-24 years	52	58.2%	156	45.5%	*Ref.*	*Ref.*		
25-34 years	45	41.7%	150	43.7%	1.11 (0.70-1.75)	0.652		
>35 years	11	10.2%	37	10.8%	1.12 (0.53-2.36)	0.763		
Mother reads English								
Easily	52	48.6%	197	57.3%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	42	39.3%	136	39.5%	0.85 (0.54-1.35)	0.505	1.14 (0.69-1.88)	0.602
Not At All	13	12.2%	11	3.2%	0.22 (0.09-0.53)	0.001	0.38 (0.14-0.99)	0.047
Maternal education								
0-8years	67	65.1%	162	47.9%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
9-12years	34	33.0%	152	45.0%	1.85 (1.16-2.95)	0.010	1.52 (0.92-2.52)	0.105
>12years	2	1.9%	24	7.1%	4.96 (1.14-21.6)	0.033	9.57 (1.23-74.5)	0.031
Marital status								
Single/Divorce	23	21.3%	52	15.1%	*Ref.*	*Ref.*		
Monogamous Married	78	72.2%	260	75.6%	1.47 (0.85-2.56)	0.168		
Polygamous Married	7	6.5%	32	9.3%	2.02 (0.78-5.25)	0.148		
Children < 5 years old in house								
≤1	44	41.1%	150	43.7%	*Ref.*	*Ref.*		
2	49	45.8%	131	38.2%	0.78 (0.49-1.25)	0.310		
≥3	14	13.1%	62	18.1%	1.30 (0.66-2.54)	0.444		
Persons in household								
≤3	22	20.6%	94	27.3%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
4-5	62	57.9%	152	44.2%	0.57 (0.33-0.99)	0.048	0.64 (0.26-1.07)	0.129
6-14	23	21.5%	98	28.5%	1.00 (0.52-1.91)	0.993	1.21 (0.60-2.42)	0.593
SES Quintile[1]								
Bottom 40%	57	53.8%	110	32.0%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Upper 60%	49	46.2%	234	68.0%	2.47 (1.59-3.86)	<0.0001	2.08 (1.29-3.35)	0.003

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; SES, socioeconomic status

[1] SES derived from Principal Components Analysis of household possessions

Table 5.11 Bivariate and multivariate analyses for predictors of sending SMS in the past week in mothers with infants ages 12-23 months old

Characteristic	Doesn't Send		Send SMS		Unadjusted OR		Adjusted OR	
	N	%	N	%	OR (95%CI)	P value	OR (95%CI)	P value
Maternal age								
15-24 years	91	43.2%	117	48.6%	*Ref.*	*Ref.*		
25-34 years	93	44.3%	102	42.3%	0.85 (0.58-1.26)	0.427		
>35 years	26	12.4%	22	9.1%	0.66 (0.35-1.24)	0.193		
Mother reads English								
Easily	101	48.3%	148	61.2%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	89	42.6%	89	36.8%	0.68 (0.46-1.00)	0.053	0.90 (0.59-1.38)	0.626
Not At All	19	9.1%	5	2.1%	0.18 (0.06-0.50)	0.001	0.26 (0.08-0.82)	0.021
Maternal education								
0-8years	124	60.8%	105	44.3%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
9-12years	74	36.3%	112	47.3%	1.79 (1.21-2.65)	0.004	1.49 (0.98-2.28)	0.063
>12years	6	2.9%	20	8.5%	3.94 (1.52-10.2)	0.005	3.24 (1.12-9.38)	0.030
Marital status								
Single/Divorce	37	17.6%	38	15.7%	*Ref.*	*Ref.*		
Monogamous Married	153	72.9%	185	76.5%	1.18 (0.71-1.94)	0.523		
Polygamous Married	20	9.5%	19	7.9%	0.93 (0.43-2.01)	0.523		
Children < 5 years old in house								
≤1	80	38.3%	114	47.3%	*Ref.*	*Ref.*		
2	93	44.5%	87	36.1%	0.66 (0.44-0.99)	0.044		
≥3	36	17.2%	40	16.6%	0.78 (0.46-1.33)	0.361		
Persons in household								
≤3	49	23.4%	67	27.7%	*Ref.*	*Ref.*		
4-5	103	49.3%	111	45.9%	0.79 (0.50-1.24)	0.306		
6-14	57	27.3%	64	26.5%	0.82 (0.49-1.37)	0.452		
SES Quintile[1]								
Bottom 40%	93	44.7%	74	30.6%	*Ref.*	*Ref.*		
Upper 60%	115	55.3%	168	69.4%	1.84 (1.25-2.70)	0.002		
Phone Ownership								
Share	122	58.1%	73	30.2%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Own	88	41.9%	169	69.8%	3.2 (2.17-4.73)	<0.0001	2.78 (1.86-4.15)	<0.0001

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; SES, socioeconomic status

[1] SES derived from Principal Components Analysis of household possessions

Table 5.12 Bivariate and multivariate analyses for predictors of sending SMS in the past week in mothers with infants ages 12-23 months old, excluding mobile phone ownership variable

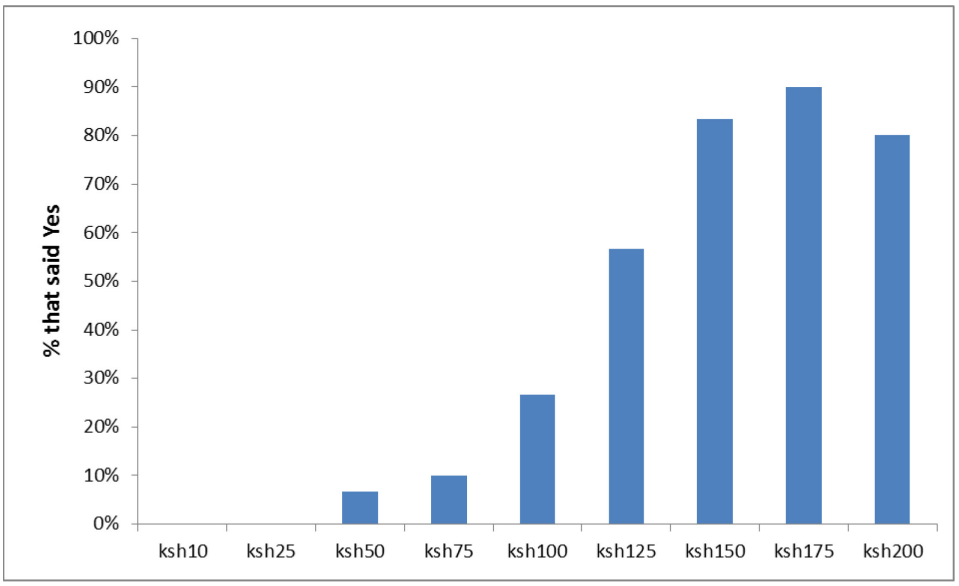
Characteristic	Doesn't Send		Send SMS		Unadjusted OR		Adjusted OR	
	N	%	N	%	OR (95%CI)	P value	OR (95%CI)	P value
Maternal age								
15-24 years	91	43.2%	117	48.6%	*Ref.*	*Ref.*		
25-34 years	93	44.3%	102	42.3%	0.85 (0.58-1.26)	0.427		
>35 years	26	12.4%	22	9.1%	0.66 (0.35-1.24)	0.193		
Mother reads English								
Easily	101	48.3%	148	61.2%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	89	42.6%	89	36.8%	0.68 (0.46-1.00)	0.053	0.87 (0.58-1.32)	0.513
Not At All	19	9.1%	5	2.1%	0.18 (0.06-0.50)	0.001	0.25 (0.08-0.78)	0.017
Maternal education								
0-8years	124	60.8%	105	44.3%	*Ref.*	*Ref.*	*Ref.*	*Ref.*
9-12years	74	36.3%	112	47.3%	1.79 (1.21-2.65)	0.004	1.45 (0.96-2.19)	0.081
>12years	6	2.9%	20	8.5%	3.94 (1.52-10.2)	0.005	3.86 (1.12-11.0)	0.011
Marital status								
Single/Divorce	37	17.6%	38	15.7%	*Ref.*	*Ref.*		
Monogamous Married	153	72.9%	185	76.5%	1.18 (0.71-1.94)	0.523		
Polygamous Married	20	9.5%	19	7.9%	0.93 (0.43-2.01)	0.523		
Children < 5 years old in house								
≤1	80	38.3%	114	47.3%	*Ref.*	*Ref.*		
2	93	44.5%	87	36.1%	0.66 (0.44-0.99)	0.044		
≥3	36	17.2%	40	16.6%	0.78 (0.46-1.33)	0.361		
Persons in household								
≤3	49	23.4%	67	27.7%	*Ref.*	*Ref.*		
4-5	103	49.3%	111	45.9%	0.79 (0.50-1.24)	0.306		
6-14	57	27.3%	64	26.5%	0.82 (0.49-1.37)	0.452		
SES Quintile[1]								
Bottom 40%	93	44.7%	74	30.6%	*Ref.*	*Ref.*		
Upper 60%	115	55.3%	168	69.4%	1.84 (1.25-2.70)	0.002		

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; SES, socioeconomic status

[1] SES derived from Principal Components Analysis of household possessions

5.7 Figures for Chapter 5

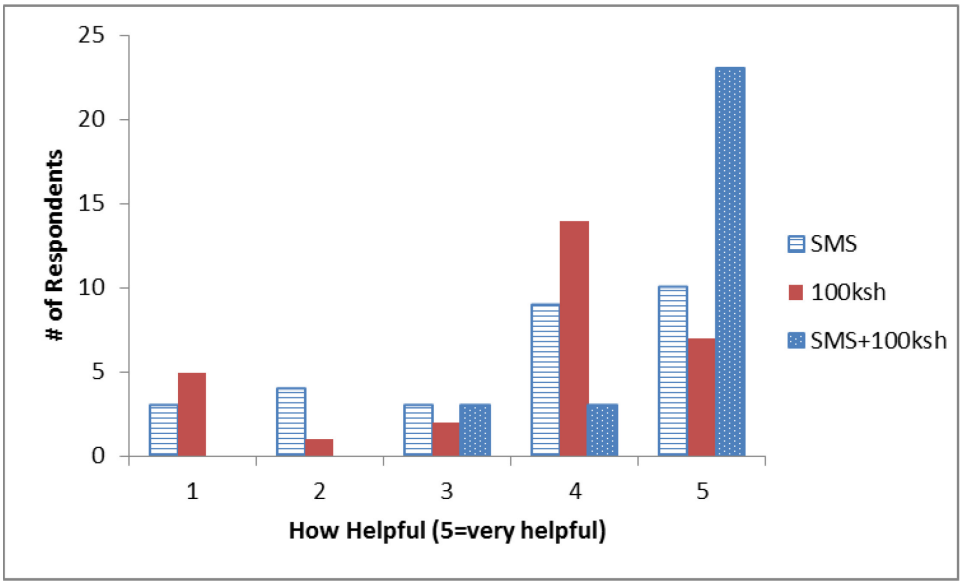
Figure 5.1 Incentive amounts that would motivate mothers to bring baby for vaccination



Abbreviation: KSH, Kenyan Schilling

CAPTION: Mothers were asked to imagine a scenario where a mother was very busy working in the garden when a community health worker approaches her and tells her that her child is due for vaccination. Study participants were asked what amount of money is needed to motivate mother to bring child for vaccination. Mothers answered privately. The incentive amounts were presented in the following order: 100ksh, 25, 200, 50, 125, 10, 75, 150, and 175; (85ksh=$1.00 USD as of October 2014).

Figure 5.2 Focus group participants ratings on helpfullness of Short Message System (SMS) and incentives to increase immunization coverage



Abbreviations: SMS, short message system; KSH, Kenyan Schilling

CAPTION: Mothers with infants ages 12-23 months were asked to privately ranks how helpful SMS reminders alone, 100 KSH incentive alone, or incentive and reminder combined at improving immunization coverage.

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Chapter 6. The Mobile Solutions for Immunization (M-SIMU) Trial: A preliminary analysis for a cluster randomized controlled trial that assesses the impact of mobile phone delivered reminders and incentives to improve timely childhood immunization in western Kenya

6.1 Abstract

Background:

Short message system (SMS) reminders and incentives are two demand side interventions that have been shown to improve healthcare seeking behaviors in lower income countries. We sought to determine if these interventions could improve timeliness of routine pediatric immunizations in rural western Kenya.

Methods:

Data for this analysis come from the first 107 infants that had 12 month follow-up visits in the M-SIMU trial, which was a four-arm, 152 cluster (village) randomized controlled trial that enrolled caregivers of infants less than 35 days old who had not initiated the pentavalent vaccine series. Villages were eligible for the study if they were within the KEMRI/CDC surveillance system and had no ongoing enhanced immunization programs or research studies. Villages were randomized with constraints in a 1:1:1:1 ratio to one of four study arms; Control, SMS reminders only, SMS reminders plus a 75 Kenyan Schilling (KSH; 85KSH=$1.00 USD) incentive or, SMS reminders plus a 200 KSH incentive. SMS reminders were sent to enrolled caregivers three days and one day before the scheduled immunization visit at 6, 10 and 14 weeks for polio and pentavalent (DTP/Hib/HepB) vaccines and at 9 months for measles vaccine. Mobile-money based incentives were sent for each vaccination if participants brought their infant for vaccination within two weeks of scheduled date for each of the four vaccination visits. Participants were not blinded to their study arm. The two primary outcomes, time to

pentavalent3 and time to measles vaccination were assessed using individual level data with adjustments for the cluster design. Inverse Kaplan-Meier (K-M) curves with log rank tests and Cox regression analyses were used to assess outcomes. Primary outcomes were also stratified by travel time to clinic and mobile phone ownership and primarily conducted with intention-to-treat analyses.

Results: Between September 30th to October 14th 2013, 107 caregivers from 53 clusters were enrolled to control (22 infants; 13 clusters), SMS (32 infants; 14 clusters), SMS plus 75 KSH (27 infants; 14 clusters), and SMS plus 200 KSH arms (26 infants; 12 clusters). The inverse K-M curves were statistically significant for differences by study arms for pentavalent3 ($p<0.01$) but not measles ($p=0.10$). Infants in the SMS plus 200 KSH were significantly associated with pentavalent3 (HR: 3.33; 95% CI: 1.71-6.47) and approached significance for measles vaccination (HR: 2.05; 95% CI: 0.95-4.41; $p=0.07$), as compared to controls. The SMS only and SMS plus 75KSH were not significantly associated with either of the primary outcomes.

Discussion: Infants of caregivers who received SMS reminders plus 200 KSH incentives ($2.25) were significantly more likely to receive timely pentavalent3 and measles vaccines. Monetary incentives and mobile phone technologies may improve timely immunization coverage estimates in resource-constrained settings.

6.2 Introduction

The decade from 2010-2019 has been dubbed the "Decade of Vaccines" with renewed focus on immunization by major international groups like WHO, UNICEF, the Global Alliance for Vaccines and Immunizations (GAVI) and the Bill and Melinda Gates Foundation.[1-3] A key component in the Global Vaccine Access Plan (GVAP) is the recognition that both demand and supply side deficiencies need to be addressed in order to achieve universal immunization.[4] Ensuring more infants receive timely vaccination is a major component in efforts to reduce child mortality by two-thirds and achieve Millennium Development Goal 4.[5] Every year, immunization programs are estimated to save over 2.5 million lives globally[6] with the majority of deaths averted occurring in Africa.[7]

Kenya's Division of Vaccine and Immunization (DVI) recommends infants receive bacillus Calmette–Guerin (BCG) vaccine at birth, three doses of polio and pentavalent (diphtheria, tetanus toxoid, pertussis, hepatitis B, and *Haemophilus influenzae Type B* antigens) vaccines at 6, 10, and 14 weeks of age, and the measles vaccine at nine months of age.[8] Data from successive Kenyan Demographic and Health Surveys (DHS) found improvements in pentavalent3 coverage from 72% in 2003, to 86% in 2009.[9] As global pentavalent coverage estimates continually improve[10, 11], timely vaccination is garnering more attention.[12, 13] Recent study site estimates found that 24% and 29% of infants had delays greater than one month for pentavalent3 and measles vaccination (Chapter 4 of dissertation).

Timely vaccination, although often overlooked in routine immunization reporting systems, is important for several reasons. First, pediatric vaccines protect against

diseases that often have highest morbidities and mortalities at earlier stages of life. Delays in vaccination have been associated with cases of pertussis, hepatitis B, and *Haemophilus influenzae* type b.[14-17] Second, delayed vaccination lessens the population's theoretical maximal herd immunity.[18] Herd immunity is important because it protects those that are too young to be vaccinated, are medically contraindicated, or do not produce a successful to immune response to vaccination.[19] Lastly, numerous studies have found that United States infants with delayed first vaccination are at higher risk of not receiving future vaccinations[20-23], with the finding being recently replicated in Kenya where infants receiving the first dose of pentavalent vaccine four weeks late were approximately 5 and 2 fold times higher to not be vaccinated with pentavalent3 and measles, respectively (Chapter 4 of dissertation)

Two potential demand-side strategies that could address deficiencies in immunization coverage and timeliness are short message system (SMS) immunization appointment reminders and small monetary incentives conditioned on timely vaccination. SMS reminders for pediatric and adolescent immunizations have been found to modestly improve immunization uptake in an urban New York City population.[24-26] In sub Saharan Africa, SMS reminders have been shown to improve HIV treatment adherence[27, 28], HIV testing[29], treatment of pediatric malaria[30], antenatal care attendance[31], institutional delivery[32], and post-circumcision clinic visits[33], but have not been tested for their efficacy on pediatric immunization uptake. In regards to incentives and immunization, two studies conducted in India and Pakistan found that providing either small food rations or food coupons improved timely immunization.[34, 35]

The objectives of this pilot analysis of a cluster randomized controlled trial are to test whether mobile phone short SMS reminders, either with or without mobile-phone based incentives, can improve the timeliness for third dose of pentavalent vaccine (pentavalent3) and measles vaccine.

6.3 Methods

6.3.1 Study Setting

The study was conducted in Gem and Asembo Districts of Nyanza Province, Kenya. Gem and Asembo are two of three districts that the Kenyan Medical Research Institute and Centers for Disease Control and Prevention (KEMRI/CDC) Health and Demographic Surveillance System (HDSS) operate in. The HDSS has systematically collected information on births, deaths, migration, morbidity and demographics every four months for a population of over 220,000 people since 2001[36]. The HDSS has previously served as a platform for other scientific studies, including randomized controlled trials for bed-net and rotavirus vaccine efficacies.[37, 38]

The study area has high levels of HIV transmission, malaria, and tuberculosis.[39, 40] Primary occupations include fishing, subsistence farming, and wage labor. Historically, Nyanza Province has the worst health and socio-economic status of Kenya's seven provinces.[9] The landscape is comprised of slowly rolling hills, pockmarked with compounds, consisting of two to six households, and surrounded by personal farm plots.

This research trial was a collaborative effort of members at the International Vaccine Access Center (IVAC) at Johns Hopkins Bloomberg School of Public Health and the Kenyan Medical Research Institute and Centers for Disease Control and Prevention (KEMRI/CDC).

6.3.2 **Study Design and Participants**

The study is a four-arm cluster randomized controlled trial whose primary outcome is to compare the efficacy of the interventions on pentavalent3 and measles vaccination. Villages, as defined by the KEMRI/CDC HDSS, are the clusters that were randomized. Villages were included in the trial if they were located in Gem or Asembo District and did not have any current immunization studies or other programs that may influence health care seeking behavior.

One hundred and fifty two villages were randomized to one of four study arms in a 1:1:1:1 allocation ratio (Figure 6.1). The study arms include: (1) Control; (2) SMS reminders; (3) SMS reminders plus 75 Kenyan Schillings (KSH); and (4) SMS reminders plus 200KSH (85 KSH=1USD as of October 2014). SMS reminders were sent both three days and one day before immunization doses scheduled at 6 weeks, 10 weeks, 14, weeks, and 9 months. Incentives were delivered to the participant's mobile phone if the participant's child was brought for immunization within two weeks of the scheduled date. All eligible mothers/caretakers residing within a study village were be assigned to the study arm that the village was allocated.

Eligible caregivers and their newborns were identified by village reporters who are casually employed by KEMRI/CDC HDSS to identify births, deaths, and pregnancies within their community. For each birth notification, KEMRI/CDC community interviewers visited the newborn's compound to explain the trial and screen the mother/caretaker. Mothers-infant pairs were eligible if the infant was less than 35 days at age of enrollment, a self-identified resident of a study village, willing to attend an M-SIMU clinic, did not intend to out-migrate from the study area in the next six months, and

if the infant had not received the first dose of pentavalent vaccine or measles vaccine. Mobile phone ownership was neither an inclusion nor exclusion criteria. For cases where mother did not own a mobile phone, she was asked to provide a phone number where SMS reminders and incentives, if applicable, could be sent.

Both oral and written informed consent was sought by community interviewers for eligible and willing mothers. The study protocol received ethical clearance from the Scientific Steering Committee (SSC), the KEMRI-Nairobi Ethical Review Committee (ERC; SSC#2409), the Johns Hopkins University Bloomberg School of Public Health (deferred to KEMRI ERC); and the Centers for Disease Control and Prevention (deferred to KEMRI ERC). The M-SIMU cluster randomized controlled trial was conducted, and its results reported, using the Consolidated Standards of Reporting Trials (CONSORT) guidelines adapted for cluster randomized trials.[41]

6.3.3 **Randomization and masking**

The 152 villages were equally randomized to the four study arms in a public ceremony attended by village chiefs and community members September 12, 2013. The constrained randomization was conducted by a statistician at Johns Hopkins University Bloomberg School of Public Health. The randomization program iterated until 5000 acceptable randomizations were found that met the following criteria:

+/- relative 10% over all 152 villages for the means of the variables: full immunization coverage, phone ownership, distance to the nearest clinic, and village population of children 12-23 months old; where full immunization coverage (FIC) was defined as infants that received BCG, three doses of polio and pentavalent, and measles vaccine

+/- relative 25% within each region (Asembo, Gem) for the means of the variables: full immunization coverage and phone ownership.

The randomization was also stratified on region such that each study arm contained 32 villages from Gem and eight villages from Asembo region. Data for the randomization came from a baseline survey conducted within the study area in March-April 2013 (Dissertation Chapters 4 and 5).

A simple random sample of n=1000 was taken from the 5000 valid randomization sequences. The 1000 sequences were labeled with a 3-digit number, 000 to 999. Each sequence allocated 38 villages to one of four groupings (A, B, C, D). Nine soccer balls were labeled with numbers 0-9 and placed in a cloth sack. Three village chiefs each drew one labeled ball, with replacement, such that a 3 digit number was generated. Villages were placed into four groups based on the allocation sequence number drawn. Then, four soccer balls labeled with the study arms (#1.control, #2.SMS, #3. 75KSH, and #4. 200KSH) were placed in a different cloth sack. A representative from each of the four groupings drew one ball, without replacement, to determine the study arm assigned to all villages within the grouping.

Due to the nature of the intervention, participants and study staff were not blinded to participant allocation.

6.3.4 **Procedures**

Upon provision of informed consent, a community interviewer texted an enrollment SMS to the RapidSMS server, a free and open-source program, that contained the mother's village and compound number, the phone number that the mother would like to receive study SMSs, the enrolled caregiver's child's date of birth, the preferred language

to receive SMS's (English, Kiswahili, or Dholuo), and the enrolled caregiver's baby's first and last name. For mothers that did not own a mobile phone, study staff urged these mothers to notify the owner of the mobile phone that they would be receiving SMS reminders and incentives for their infant's immunization visit. After the enrollment SMS was sent, enrolled caregivers received a personalized SMS sent from the RapidSMS server that welcomed the mother to the study.

If mothers were randomized to the SMS only, SMS plus 75 KSH, or SMS plus 200 KSH arm, SMS reminders were sent to mother's identified mobile phone on both three days and one day before the scheduled immunization visits at 6, 10, and 14 weeks for the three doses of pentavalent vaccine and at 9 months for measles as per Kenyan Expanded Programme on Immunization (KEPI) guidelines (Figure 6.2).[42] If a pentavalent vaccination was given later than the scheduled date, then SMS reminders for the subsequent pentavalent dose were reprogrammed to occur at four weeks from the date of vaccine receipt, as per KEPI guidelines.

SMS reminders contained personalized wording indicating which vaccine the infant was due to receive. If the participant was in an incentive arm, the reminder also included the amount of money the caretaker would receive for vaccinating her child (within two weeks of the scheduled due date). Motivational sayings were attached at the end of the SMS. These sayings were selected as a result of focus group discussions and were randomized for each vaccine dose.

If mothers were randomized to either SMS plus 75 KSH or SMS plus 200 KSH arm, mobile phone-based monetary incentives were delivered to mother's identified mobile phone for each timely dose of pentavalent and measles vaccine, defined as within

two weeks of the scheduled date (i.e., pentavalent1 at 6 weeks, pentavalent2 and pentavalent3 four weeks after the previous dose and measles at 9 months (272 days). If the infant received vaccination two weeks after the scheduled date, no incentive was transferred. Incentives were delivered through the participant's choice of mobile network and delivered within 24 hours of vaccine receipt. The incentive amount transferred for timely vaccination was 75 KSH for those in the SMS plus 75 KSH arm and 200 KSH for those in the SMS plus 200 KSH arm. Mothers residing in control arm villages received only a welcome SMS upon enrollment. No additional SMSs or incentives were sent to mothers in the control arm.

KEMRI/CDC health facility recorders were stationed at 24 clinics to document enrolled infant's immunization. After infants were immunized, health facility recorders sent an SMS message to the RapidSMS server, which automatically calculated whether vaccine was received within two weeks of scheduled date. At the end of each working day, a KEMRI/CDC employee downloaded that day's list of incentive arm participants whose infants received timely vaccination and uploaded the file to the KEMRI Bill Pay system where the appropriate incentive was then dispensed. When infants reached 12 months of age, community interviewers conducted in-home follow up visits to document immunization coverage using either maternal and child health booklet (MCH) or verbal report.

6.3.5 **Data Collection**

Over the course of the trial, participants were interviewed up to six times. Interviews occurred at enrollment, twelve month follow up, and at each of the immunization visits for clinics staffed by M-SIMU personnel.

Enrollment surveys were collected by community Interviewers using ODK Collect software loaded on a simple smart mobile phone (Huawei Ascend Y200 model) (Appendix 10). Information collected at enrollment includes mobile phone literacy, demographics, vaccine perceptions, transportation, and socioeconomic status. Community interviewers transmitted completed surveys to a secure server at KEMRI/CDC using the local mobile phone network.

At immunization visits, health facility recorders interviewed enrolled mothers after their infant's immunization using netbook computers programmed by KEMRI/CDC staff. These surveys were designed to collect information relating to financial and non-financial costs associated with the clinic visit. Additionally, previous vaccinations were recorded if a mother presented to clinic with infant's maternal and child health booklet. Weekly, field supervisors collected the health facility recorder's netbooks and downloaded the data to a portable hard drive that was then brought to KEMRI/CDC Kisumu headquarters and stored on a secure server.

When infants were aged 11 to 12 months, community interviewers conducted in-home follow-up visits to ascertain immunization status and collect information on mothers' perceptions of intervention. Similar to enrollment surveys, the data was collected on mobile phones equipped with ODK collect software.

The RapidSMS system was programmed to generate daily logs of SMSs sent and received. Daily, quality control checks confirmed validity of the enrollment and immunization receipt. Potential errors discovered were given to the field supervisors and followed up at the field. Routinely, the logs of SMS reminders sent to mothers were examined to ensure that the intervention was being delivered in line with the protocol.

6.3.6 **Dependent variable definitions**

The two primary outcomes are pentavalent3 vaccination by 24 weeks of age and measles vaccination by 10 months of age. Data for primary outcomes were collected at follow-up visits when infant was between 11-12 months. A child was defined as vaccinated for either vaccine if there was written confirmation independent of the M-SIMU prospectively collected data from immunization clinics. Infants with maternal and child health booklet at follow-up was sufficient for determining primary outcomes, unless there was discrepancy with dates from immunization SMS records, in which case, the clinic immunization log book was used to resolve date differences. For those that orally reported at follow-up, clinic records were searched and immunization date recorded.

The infant's age at vaccination was calculated by subtracting the infant's date of birth from the date of vaccination. Infant were considered vaccinated with pentavalent3 by 24 weeks of age if the infant received the three dose pentavalent sequence before the infant aged to 168 days (24 weeks). Infants were considered vaccinated with measles vaccine by 10 months of age if the infant received measles vaccine by 302 days of age (10 months). The measles primary outcome was independent of child's pentavalent3 status.

6.3.7 **Data Analysis**

The data for this analysis came from a preliminary cohort of M-SIMU infants which includes the first 107 infants who had a 12 month follow-up visit completed. *A priori*, these infants were excluded from the formal analysis of the 2042 infants in the M-SIMU trial. This cohort was established to assess the readiness of the automated SMS and incentive delivery systems. Participants in this cohort underwent all study

procedures as those in the larger trial. Analyses were conducted using intention-to-treat (ITT) for delivery of SMS reminders. Per protocol analyses were conducted to corroborate ITT analyses.[43] For ITT analyses, the full sample of infants was analyzed for pentavalent3 and measles vaccination. Per protocol analyses of pentavalent3 vaccination were conducted for the sample of infants that had SMS reminders delivered per protocol for pentavalent1, pentavalent2, and pentavalent3 vaccines. Per protocol analyses of measles vaccination was conducted for the sample of infants that had SMS reminders delivered correctly for measles vaccine.

Cluster level and individual level estimates of baseline variables were generated for each study arm and visually inspected to see if there were any differences in study arms. Due to the large number of clusters per study arm, individual level analyses were favored over cluster level analyses due to the improved efficiency and ease of adjusting for covariates in a single step.[44]

Inverse Kaplan-Meier curves were created for the pentavalent3 and measles primary outcomes as performed elsewhere.[45-47] Infants that were alive and had not migrated from the study area were censored at 24 weeks for pentavalent3 and 302 days for measles if the vaccine was not received by the respective time points. Infants that died or migrated from study area before the vaccine was given were censored at age of death or migration if this occurred before 24 weeks for pentavalent3 and 302 days for measles vaccines. For statistical purposes, infants entered the study, or in other words were at risk for vaccination, at 12 weeks for pentavalent3 vaccine (2 weeks before pentavalent3 is recommended) and at 180 days for measles (measles can be given as early as 6 months in HIV+ infants). Log rank tests with trend option were used to assess the

global equality of inverse survival curves and differences in trends across the four study arms.[48] To assess the proportional hazards assumption for Kaplan-Meier survival analysis, log-log plots were created and visually assessed for parallel curves.[49] Additionally, the proportional hazard assumption for Cox regression models was tested based on examination of Schoenfeld residuals and log-log plots.[50]

Unadjusted hazard ratios for study arms on pentavalent3 vaccination and measles vaccination were obtained by Cox regressions[51] and included adjustment for the cluster design of the trial by use of robust variance estimates of immunization status at village level.[52] For adjusted Cox regression analyses, *a priori*, mobile phone ownership, region, and time to clinic were included in models using the 'strata' option to allow for different baseline hazards of covariates. Additional variables were included in adjusted Cox regressions if there were differences in their distribution by study arm and if their unadjusted Cox regression estimates were statistically significant. *A priori,* unadjusted and adjusted effect estimates for pentavalent3 and measles vaccine receipt were presented stratified separately by mobile phone ownership and time to clinic. An alpha of 0.05 was used for all hypothesis testing. Analyses were performed using STATA/IC, version 11.2 (Stata Corp, College Station, Texas).

6.4 Results

Enrollment for the pilot sample occurred from September 30th to October 14th 2013, where 138 birth notifications from 61 villages were received by study staff. Twenty-six mother-infant pairs did not meet eligibility criteria, 3 mothers refused, and 2 infants died before study staff could approach mothers for enrollment (Table 6.1). A total of 107 mothers with eligible infants from 53 villages were included in the preliminary cohort

(Figure 6.1). The number of infants (clusters) enrolled in control, SMS, SMS plus 75 KSH, and SMS plus 200 KSH arms were 22 infants (13 clusters), 32 infants (14 clusters), 27 infants (14 clusters), and 26 infants (12 clusters), respectively. The average cluster size of enrolled infants for control, SMS, SMS plus 75 KSH, and SMS plus 200 KSH arms were 2.3, 3.1, 2.6, and 2.6 infants respectively. One infant in the 200 KSH arm migrated from the study area and could not have immunization records confirmed and was considered lost to follow up. The following are results for 106 infants with independently confirmed immunization status.

6.4.1 **Baseline Characteristics**

The present sample represents infants from 53 of the 152 villages that were randomized with restrictions on village size, socioeconomic status, mobile phone ownership levels, and full immunization coverage levels. The variables that were restricted for randomization come from a baseline survey conducted in March of 2013. Cluster estimates, weighted for number of infants, of mobile phone ownership, full immunization coverage, socio-economic status, and straight line distance to the nearest clinic were similar across the four study arms (Table 6.2). The control arm had a higher cluster proportion of infants from villages in Asembo District (50%) as compared to the SMS (78%), lower incentive (85%), and higher incentive (76%) arms. The SMS arm had smaller average cluster size (17 infants), defined as the 2012 birth cohort for that village, as compared to the control (26 infants), lower incentive (27 infants), and higher incentive (23 infants) arms.

Individual baseline characteristics of the sample are presented in Table 6.3. Maternal age, maternal education, marital status, number of antenatal visits in last

pregnancy, number of children under 5 years old regularly sleeping in the household, number of people in the household, and age of infant at enrollment were similar across the four study arms (intention-to-treat). Infants in the lower and higher incentive arms had lower levels of health facility deliveries, 56% and 64% respectively as compared to control and SMS arms, 82% and 75% respectively. Additionally, infants in the lower and higher incentive arms had lower levels of mobile phone ownership, 37% and 40% respectively as compared to control and SMS arms, 73% and 69% respectively. The higher incentive arm had a higher proportion of female infants, 76%, as compared to control (46%), SMS only (38%) and lower incentive arms (48%). Infants in SMS only and higher incentive arms had higher proportions of travel time to the clinic exceeding thirty minutes, 50% and 28% respectively, than those in the control and lower incentive arm, 9% and 11% respectively. Baseline SMS behavior, which included regularly receiving and sending SMS, and the number of messages sent or received per week were similar across the study arms (Table 6.4).

6.4.2 **Delivery of SMS reminders**

Overall, for the 84 infants who were in SMS only and SMS plus incentive arms, 92.6% of SMS reminders were delivered per protocol for the pentavalent1, pentavalent2, pentavalent3, and measles vaccines (Table 6.5). Vaccine specific estimates found that 96%, 86%, 94%, and 96% were delivered per protocol for pentavalent1, pentavalent2, pentavalent3, and measles vaccines, respectively. There was little difference in per protocol delivery of SMS reminders by study arm, with 95%, 92%, and 91% of reminders in SMS only, SMS plus 75KSH, and SMS plus 200KSH delivered correctly.

The number of vaccinations that were correctly sent reminders is presented in Table 6.6. Overall, 69 of the 84 infants (82%) in SMS and incentive arms had reminders delivered as intended, with 8 (10%) of infants having reminders delivered for three of the four vaccines. Four infants (5%) had reminders delivered correctly for two of the four vaccines and 3 infants (4%) had reminders delivered correctly for one vaccine. At least one reminder was delivered correctly to all infants. The distribution of correctly delivered SMS reminders was similar by study arm. For SMS only, SMS plus 75 KSH, and SMS plus 200 KSH, 85%, 81%, and 80% of infants had all reminders delivered protocol.

6.4.3 **Effect of interventions on timely pentavalent3**

Intention-to-treat analyses utilized the full sample of 106 infants for pentavalent3 vaccination by 24 weeks. Per protocol analyses utilized data from 91 infants; 15 infants were excluded because SMS reminders were not delivered correctly for all three doses of pentavalent vaccines.

Log-log plots were assessed for violation of proportional hazards assumption (Figure 6.3). There was an overall significant difference in inverse Kaplan-Meier curves by study arm for time to pentavalent3 vaccination in both intention-to-treat (Figure 6.4) and per protocol analyses for delivery of SMS reminders (Figure 6.5), with a significant trend in survival curves, going from control, to SMS only, to SMS plus 75 KSH, to SMS plus 200 KSH ($p<0.01$). The SMS plus 200 KSH inverse survival curve was significantly different than the SMS plus 75 KSH curve with no difference in curves between the SMS and control arms in both per protocol and ITT analyses. The median ages for pentavalent3 vaccination by study arm were: SMS plus 200 KSH (101 days,

95%CI 99-103 days), SMS plus 75 KSH (107 days, 95%CI: 103-110 days), control (111 days, 95%CI: 101-119 days), and SMS arm (116 days, IQR: 106-120 days). Control arm infants had greatest variance in median days to pentavalent3 vaccination. There was no difference in survival curves of pentavalent3 vaccination for potential covariates and stratified variables (Appendix 11). In infants that reached 24 weeks of age, pentavalent3 coverage was 95.5% (77.1%-99.9%), 89.7% (72.6%-97.8%), 88.9% (70.8%-97.6%), and 100% (85.8%-100.0%), in control, SMS only, SMS plus 75KSH, and SMS plus 200KSH arms, respectively.

Cox regression analysis of pentavalent3 vaccination found that participants in the SMS plus 200 KSH arm were more likely to receive pentavalent3 than infants in control arms in unadjusted (HR: 2.95; 95% CI: 1.69-5.16) and adjusted (aHR: 3.33; 95% CI: 1.71-6.47) intention-to-treat analyses (Table 6.7). Those enrolled in SMS only and SMS plus 75 KSH arms were not significantly more likely to receive pentavalent3 than control arm infants. The results of per protocol adjusted analyses had similar statistical findings to ITT analyses, SMS plus 200KSH (aHR: 3.89; 95%CI: 1.88-8.02).

6.4.4 **Effect of timely interventions on measles vaccination**

Intention-to-treat analyses utilized the full sample of 106 infants for measles vaccination by 10 months of age. Per protocol analyses utilized data from; five infants were excluded from per protocol analyses of measles coverage because reminders were not delivered for measles vaccine correctly.

There was no significant difference in time to measles vaccination by study arm in intention-to-treat (p=0.10) and per protocol analyses (p=0.14), (Figure 6.6 and 6.7) The median age for measles vaccination in study arms were: control (279 days, 95%CI: 273-

295), SMS only (285 days, 95%CI: 275-295), SMS plus 75KSH (283 days 95%CI: 275-297), SMS plus 200 KSH (277 days, 95%CI: 275-282). There was no difference in survival curves of measles vaccination for potential covariates and stratified variables (Appendix 12). In infants that reached 10 months of age, measles coverage was 81.8% (59.7%-94.8%), 71.4% (51.3%-86.8%), 72.0% (50.6-87.9%), and 95.8% (78.9%-99.9%), in control, SMS only, SMS plus 75KSH, and SMS plus 200KSH arms, respectively.

Although, there were no significant findings for unadjusted Cox regression analyses of measles vaccination by study arm in intention-to-treat analyses (Table 6.8), infants in the SMS plus 200 KSH arm trended towards statistical significance as compared to control (HR: 1.57; 95% CI: 0.86-2.89; p=0.14). Similarly, estimates approached statistical significance in adjusted ITT analyses (aHR: 2.05; 95% CI: 0.95-4.41; p=0.07) and adjusted per protocol analyses (aHR: 2.01; 95% CI: 0.95-4.26; p=0.07). SMS only and SMS plus 75KSH were not significant in unadjusted and adjusted models.

6.4.5 **Subgroup analyses**

In stratified analyses of mobile phone ownership, we found some evidence for effect modification of pentavalent3 vaccination (Table 6.9). Infants in the SMS plus 75 KSH arm were significantly associated with pentavalent3 vaccination in adjusted ITT analyses of mobile phone owners (aHR: 2.83; 95%CI 1.19-6.72) but not for those without a mobile phone (aHR: 1.05; 95%CI 0.37-3.00; p=0.93). Effect estimates of those in SMS plus 200 KSH arms were similar for those that own a mobile phone (aHR: 4.48; 95%CI 2.05-9.75) and those that do not (aHR: 3.89; 95% CI 1.22-12.4). Infants in SMS only arm did not have significant effects in either those that own mobile phones or those that

do not, although statistical significance was approached in per protocol analyses of mobile phone owners (aHR: 0.55; 95%CI: 0.28-1.08; p=0.09).

In stratified analyses of travel time to clinic (Table 6.10), we found some evidence for effect modification of pentavalent3 vaccination. Infants living less than 30 minutes from clinic and in the SMS plus 200 KSH arm were significantly associated with pentavalent3 receipt in unadjusted (HR:3.60; 95% CI: 1.91-6.76) and adjusted ITT analyses, (aHR:3.47; 95% CI: 1.67-7.20), but were not significant if living greater than 30 minutes away. There was no effect in SMS only and SMS plus 75 KSH in either of the time to clinic categories, although infants in SMS only and living greater than 30 minutes from clinic trended towards non-vaccination (aHR: 0.31; 95% CI 0.08- 1.22; p=0.10.

In stratified analyses of mobile phone ownership and measles vaccination (Table 6.11), we found some evidence for effect modification. Infants in the higher incentive arm with caregivers that owned mobile phones were more likely to receive measles vaccination in unadjusted, (HR: 2.84; 95% CI: 1.37-5.88), and adjusted ITT analyses, (aHR: 3.02; 95%CI 1.49-6.14), with null findings in those that do not own mobile phones. There was no effect in either of mobile phone ownership categories for infants in SMS only and SMS plus 75KSH arms.

In stratified analyses of travel time to clinic and measles vaccination, we found some evidence for effect modification (Table 6.12). Infants living less than 30 minutes from clinic and in the SMS plus 200 KSH arm were significantly associated with measles receipt in unadjusted, (HR:2.12; 95% CI: 1.15-3.90), and adjusted ITT analyses, (HR:2.41; 95% CI: 1.11-5.23), but were not significantly associated with measles vaccination in infants that live greater than 30 minutes from the clinic. There were no

significant findings for SMS only and SMS plus 75 KSH infants in either those that live closer or farther from a clinic.

6.5 Discussion

In this cluster randomized controlled trial, SMS immunization reminders coupled with the higher 200 KSH incentive was significantly associated with pentavalent3 vaccination and approached statistical significance for measles vaccination. Stratified analyses found a positive effect of the higher incentive arm for pentavalent3 in those who own and those who do not own a mobile phone, and in mothers who live less than 30 minutes to the clinic. The higher incentive arm, in stratified analyses, also showed a significant effect on measles outcome in those who own mobile phones and those who live closer to the health facility. For infants of villages randomized to SMS plus the lower 75 KSH incentive, there was no effect on either of the primary pentavalent3 and measles outcomes, however, there was an observed effect modification for mobile phone ownership. Infants of villages randomized to the SMS only arm showed no significant associations in primary and stratified analyses of pentavalent3 and measles vaccines with the exception of stratified analyses of pentavalent3 where infants living greater than 30 minutes from the clinic were significantly less likely to be vaccinated as compared to controls in adjusted per protocol analyses.

There is substantial evidence that small incentives can produce positive behavior change in developed countries[53-55], including strong evidence for adult immunizations[54], with insufficient evidence for pediatric[56, 57] and adolescent vaccines.[58] Our finding that the provision of financial incentives improved timely immunization is consistent with

results from developing countries and also from the few studies that employed monetary and non-monetary incentives, such as food rations or vouchers, to yield positive behavior change in lower income countries.[34, 35, 59, 60]

Although the 200 KSH incentive arm showed positive associations with most of the primary and stratified outcomes, the 75 KSH arm did not. A previous study in rural Malawi randomized individuals to vouchers ranging from $0 to 3 USD that were redeemable if HIV test results were obtained from a testing clinic.[59] The authors found that very small incentives (e.g. <$0.20) induced high uptake of HIV test results (>65%) as compared to controls (35%) and that there were marginal gains in testing uptake with increasing incentives beyond $1.00. A trial from rural Kenya randomized uncircumcised males to control groups, $2.50 USD incentive, $8.75 incentive, and $15.00 incentive, where incentives were given if the participant was circumcised within two months.[60] The authors found no effect of the smallest incentive on circumcision uptake, but found significant effects in those receiving the $8.75 and $15.00 incentives. Our study results are more consistent with the latter study's as the provision of smaller incentive amount did not elicit behavior change, while the higher incentive did.

Far distances to the clinic have frequently been associated with poor immunization coverage levels.[61-72] The purpose of incentives in this trial was to help alleviate the burden of transport costs associated with longer travel by serving as a form of travel subsidy. In the Malawi HIV testing study, there was some evidence that the incentives' efficacy was greater in those living farther distances from the testing site, than those living closer.[59] Our study yielded conflicting results, with the highest incentive only effective in those living closest to the health facility. Our null finding for longer

travel times may be explained by the incentive amount not sufficient to cover transport costs, thus not reducing the direct and opportunity costs in caregiver's internal cost-benefit calculations of whether to bring their infant for immunization. Moreover, behavioral economics reveals that individuals place greater value and emphasis on cost-benefits that are immediate, such as treatment, as compared to those that are delayed, such as preventive medicine.[73]

This trial was designed and implemented as an effectiveness study, with mobile phone ownership not being a prerequisite for enrollment, unlike other SMS reminder randomized controlled trials conducted in sub Saharan Africa.[27, 33, 74, 75] Mobile phone ownership in low income countries is growing rapidly[76, 77], yet ownership is still concentrated in wealthier, more educated, men.[78-80] Study site-specific data from March 2013 indicate that access to a mobile phone within the compound approached 100%, but only approximately half of mothers own a mobile phone, with older, more educated, wealthier females more likely to own a phone than to share (Dissertation Chapter 5). In light of low mobile phone ownership levels, we still intentionally decided to enroll mothers independent of mobile phone ownership, with the expectation that the 'local economy' would sort itself out and that mothers not owning a mobile phone would find someone they know to relay SMS reminders and incentives.

The findings of mobile phone ownership level and being immunized were mixed. The effect estimates for the higher incentive arm in mobile phone owners and sharers were similar for pentavalent3 while infants in the smaller incentive arm were only significantly associated with mobile phone owners. Similar to the explanation for the null finding of stratified travel time analyses, it is possible that the 75KSH incentive was

too small to motivate individuals to relay the reminder message and incentive to enrolled mothers who do not own a mobile phone, with the 200KSH incentive amount being sufficiently high enough to promote the relaying of reminders and incentives.

For measles vaccine, the higher incentive was associated with mobile phone ownership, but not mobile phone sharing in stratified analyses. Unlike pentavalent3, there was no effect of the smaller incentive in both mobile phone owners and mobile phone sharers. Since the pattern of results is different in pentavalent3 and measles, it is possible that the vaccine schedule may have impacted the results. Briefly, if someone receives pentavalent3, it is possible they had already received two incentive payments for timely vaccination of pentavalent1 and pentavalent2. Moreover, these incentives would have been received between 6 and 10 weeks of age, with infants' average age at enrollment being 3 weeks. Where pentavalent3 benefits from a combination of both a short time from enrollment to the pentavalent vaccine series and successive incentives in a short period, the measles vaccine is given at 9 months of age, or 6 months after a timely pentavalent3 dose, which may be a long enough time for the effect of incentives to be 'unlearned' by both mobile phone owners and sharers and potentially may explain why incentives were associated with mobile phone owners for pentavalent3, but not measles.

The lack of significant association between those in SMS only arms and the primary outcomes in ITT and per protocol analyses contradicts with the majority of findings for SMS reminder randomized controlled trials conducted in sub Saharan Africa. Of these ten trials, with health outcomes ranging from HIV treatment adherence to antenatal care attendance, eight studies found small, but significant effects of SMS reminders as compared to controls.[27-33, 81] Acknowledging the heterogeneity in health

behaviors studied, participants randomized to SMS reminders had absolute differences between SMS and control arm ranging from 6 to 24%. Two studies found no significant effect of SMS reminders.[74, 75] In one study, SMS reminders had no effect on early resumption of sexual activities following voluntary male circumcision[75]. The second study found no effect of SMS reminders on HIV treatment adherence[74], but two other studies with similar outcome found a pooled 22% reduction in treatment adherence failure significant in those randomized to SMS reminders.[27, 28, 82]

The success of SMS reminders to illicit a behavior is likely multifactorial; the content of the message, the type of behavior being reminded, indirect and direct costs incurred, literacy level, and other contextual factors all being potential explanatory factors. SMS reminders may also not be effective, or even not needed, when the targeted population places high importance on the behavior and already has high levels baseline levels. A baseline survey of 1748 mothers with immunization cards for infants ages 12-23 month old found high coverages of pentavalent1 (99%), pentavalent3 (95%), and measles (83%) vaccine with respective proportions of infants immunized within 1 month of the scheduled date being 90%, 76%, and 71% (Dissertation Chapter 4). SMS reminders target the caregiver's forgetfulness of infant's immunization appointments or provide knowledge if the vaccination schedule is not known. With high coverage and adequate levels of timeliness, there are likely other explanatory variables of not being immunized that SMS reminders cannot address.

We favored the use of a cluster randomization over an individual randomization for several reasons. In an individually randomized trial, neighbors, or even people living in the same compound could receive different payment amounts or no incentive at all.

The cluster design should minimize this source of discord. Similarly, in the scenario of neighbors where one receives an incentive and the other nothing, the provision of an incentive may serve as a disincentive for the decision to bring infants for vaccination by mothers who received nothing. Moreover, the cluster design lessens the chance of study arm contamination.

We chose to use survival curves and Cox regression as our primary method of analysis because it most robustly captures the time-to-event data. Relative risk or odds ratio at 24 weeks for pentavalent3 and 10 months for measles vaccination would result in a loss of all the individual time point-events before the cut-off point. An important consideration in the interpretation of the hazards ratios presented here is that because of some minor violations in the assumption of proportional hazards, and particularly located in the tail of the curves, the estimates considered an 'average hazard ratio' for the length of follow-up time.[83] Relative risks for coverage estimates of pentavalent3 vaccination at 24 weeks and measles vaccination at 10 months, as well as risk ratios for vaccination within two weeks of the scheduled date for all pentavalent vaccines and measles vaccine are located in appendices 13-15.

This study has several strengths. First, SMS reminders were sent according to protocol for the majority of infants which makes interpretation of results more generalizable. Second, by enrolling infants at birth, selection bias was minimized when compared to enrolling from the clinic. Enrollment of infants before their first vaccination ensures the population was validly represented by including infants who might not go for any vaccines. If we had enrolled from the clinic, this subset of the population would not have been represented. Lastly, this trial was conducted in a way such that the results

could be interpretable if brought to scale within Nyanza Province. Mother-caregiver pairs were enrolled independent of mobile phone ownership and there was minimal interference with participant's care seeking behaviors as household visits were only conducted at enrollment and 12 month follow-up.

The study also had several limitations. The parent M-SIMU trial requires 1972 infants to have sufficient power to detect an absolute 15% difference level in proportions of fully immunized children (BCG, 3 doses of polio, 3 doses of pentavalent, and measles vaccine) in comparison of intervention to control arms. The present pilot analysis is limited by its small sample size and therefore its findings should be interpreted cautiously. For pentavalent3 and measles vaccination, we had approximately 50% power to detect a hazard ratio of at least 2.0 for primary outcomes (Dissertation Chapter 3). Second, although we have records of SMS reminders being delivered correctly, we do not have complete information on whether SMS reminders were received and opened, or relayed in the case of those sharing mobile phones. This information would be useful for per protocol analyses, although not as important when considering the trial was designed to be an effectiveness study. Third, this study would benefit from either individual or group discussions of caregivers' opinions about receiving SMS reminders and incentives. This information would be useful in explanations for why SMS reminders were not effective at improving timely immunization. Lastly, caution should be taken when generalizing these results to other countries and settings. Our rural study area has high baseline immunization levels, moderate levels of mobile phone ownership[79], and a widespread mobile-money network.[84, 85] Although SMS reminders alone were not effective in this pilot analysis, SMS reminders may be effective in areas with lower levels

of immunization coverage, as forgetfulness and lack of knowledge surrounding vaccination schedule may be more important.

Similarly, some may question the feasibility of replicating this trial in settings where mobile phone ownership is lower and mobile-money systems are lacking. We counter that the components of the intervention can be disaggregated into individual modules (SMS reminders, incentives, and mobile-money) and be applied based on a country's available technology. For example, instead of transferring cash via mobile-money, incentives can be given by providing mobile phone airtime or even cash vouchers. Mobile money was used in this trial because of its widespread acceptance and it replaces the need to have physical cash at a health facility where it may either be lost or stolen.

As the use of economic incentives becomes more widespread, there have been considerable discussions regarding the ethics of incentivese[86-89], with arguments both for[90] and against their use.[91] The incentive amounts in this study are small, less than one day's working wage[60], and for the majority of participants, did not fully cover transportation costs. Moreover, our use of incentives was not aimed at a risky or dangerous behavior, as pediatric immunization is a routine, healthy behavior and is standard of care. If incentives can drastically improve immunization coverage and timeliness, the subsequent higher herd immunity levels would confer health and economic benefits (associated from not needing to go to the clinic for a vaccine-preventable disease) to other people who do not receive incentives. Recent economic analyses argue that increasing access and coverage levels of six pediatric vaccines (pneumococcal, *Haemophilus influenzae* type b, rotavirus, pertussis, measles, and

malaria) in seventy two lower income countries, 6.4 million lives of children could be saved[92] with economic savings associated with treatment cost and productivity loss totaling over 200 billion US dollars.[93]

A common critique of incentives centers on sustainability and scalability concerns. To address these concerns, first, additional highly powered studies are needed before recommending incentives as a panacea for improving immunization rates. If incentives are not effective, or are modestly effective but cost-effective analyses argue against their use, then incentives should not be brought to scale. Aside from the economic benefits associated with treatment cost and loss of productivity[93], the use of incentives, at least in our study area, could theoretically be cost-effective, or even cost-neutral, by savings in labor and transport costs associated with a reduction in monthly vaccination camps, catch-up campaigns, and other supplemental routine immunization activities if incentives improve clinic attendance for routine vaccinations. Moreover, economic incentives could be selectively targeted to districts with poor immunization rates or to caregivers of infants who are late for first dose of pentavalent vaccine. Previous work from this study site has found that in the 10% of infants who received pentavalent1 4 weeks late, these infants had a 2 fold increase in risk of not receiving all routine immunizations as compared to those who were received pentavalent1 timely (Dissertation Chapter 4). A targeted approach of delivering incentives within Kenya is not novel. The Government of Kenya's Cash Transfer for Orphans and Vulnerable Children (Kenya CT-OVC), active since 2007, provides $20 USD monthly to poor households of orphans or chronically ill parents.[94]

Lastly, there is some concern about a potential negative rebound effect in immunization rates if incentives are no longer given (i.e. will immunization rates decrease after incentives are no longer provided). This concern is grounded on the notion that the extrinsic reward of incentives crowds out the intrinsic reward of bringing your infant for immunization because it is healthy for the infant. Although there is some evidence for this effect in higher income settings[95], we believe it may not hold true for immunization seeking behavior in rural Kenya. First, incentives are used for all vaccines an enrolled infant would receive. The study is set within the KEMRI/CDC surveillance system which affords an opportunity to examine immunization rates of subsequent children who are not incentivized. Second, the behavior incentivized is routine. Third, focus group discussions and high baseline immunization levels suggest that caregivers place high intrinsic value in immunizing their infants. Fourth, the consequences of not vaccinating are very real for our study participants, evidenced by high levels of under 5 year mortality caused by vaccine preventable diseases.[96] Still, caution on use of incentives is required and their implementation should be carefully monitored.

In conclusion, small monetary incentives delivered to caregivers of infants upon completion of timely immunization led to timelier vaccination for pentavalent3. While the smaller incentive, $0.85 (75KSH) did not strongly elicit changes in immunization seeking behaviors, the provision of a $2.25 incentive (200KSH) did, with the effect observed in caregivers who own mobile phones and of those who share. Although SMS reminders were not observed to have significant effects on timely pentavalent3 and measles vaccination rates, their future use in other populations should not be discounted

as this study had small sample size and a population exhibiting high levels of timely immunization.

6.6 Tables for Chapter 6

Table 6.1 Summary of enrollment, refusals and exclusions for pilot phase of M-SIMU trial

	Control		SMS		75 KSH[1]		200 KSH[1]		Total	
	n	%	n	%	n	%	n	%	n	%
Households Visited	28	100	38	100	35	100	37	100	138	100
Enrolled	22	78.6	32	84.2	27	77.1	26	70.3	107	77.5
Refusals	0	0.0	0	0.0	2	5.7	1	2.7	3	2.2
Excluded	5	17.9	5	13.2	6	17.1	10	27.0	26	18.8
Child >35 days	3	10.7	4	10.5	6	17.1	7	18.9	20	14.5
Doesn't live in study village	0	0.0	0	0.0	0	0.0	2	5.4	0	0.0
Won't bring to M-SIMU clinic	2	7.1	1	2.6	0	0.0	1	2.7	2	1.4
Received pentavalent1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Moving in next 6 months	0	0.0	0	0.0	0	0.0	0	0.0	4	2.9
Died before screening	1	3.6	1	2.6	0	0.0	0	0.0	2	1.4

Abbreviations: SMS, short message system; KSH, Kenyan Schilling; M-SIMU, mobile solutions for immunization

[1] 85 KSH= 1 United States Dollar as of October 2014

Table 6.2 Cluster level summaries of baseline data for villages included in pilot analysis, weighted for cluster size

Variable	Control Mean (95%CI)	SMS Mean (95%CI)	75 KSH[1] Mean (95%CI)	200 KSH[1] Mean (95%CI)
Number of clusters	13	14	14	12
Cluster size[2]	2.3 (1.8-2.8)	3.1 (2.5-3.6)	2.6 (2.0-3.1)	2.6 (2.2-3.0)
Region-Asembo[3]	50.0% (28.2%-71.7%)	78.2% (60.0%-90.1%)	85.2% (66.3%-95.8%)	76.0% (54.9-90.6%)
Full Immunization Coverage[3,4]	84.7% (77.7%-91.6%)	79.7% (73.1%-86.4%)	82.5% (77.9%-87.1%)	87.8% (83.8%-91.8%)
Mobile phone ownership[5]	60.1% (55.3%-64.9%)	56.4% (52.4%-60.3%)	58.6% (53.4%-63.8%)	52.6% (46.6%-58.5%)
Socioeconomic status[4]	3.16 (2.93-3.39)	3.01 (2.90-3.12)	2.91 (2.83-2.99)	2.90 (2.72-3.09)
Village Size[6]	26.3 (22.1-30.6)	17.3 (15.1-19.5)	27.4 (22.0-32.8)	23.2 (19.9-26.6)
Distance to nearest clinic (km)	1.27 (0.92-1.63)	1.80 (1.53-2.07)	1.58 (1.34-1.83)	1.44 (1.18-1.69)

Abbreviations: SMS, short message system; KSH, Kenyan Schilling

[1] 85 KSH= 1 United States Dollar as of October 2014
[2] Number of infants enrolled in the cluster (village)
[3] Proportions and 95% confidence intervals
[4] Full immunization coverage is proportion of infants receiving BCG, three doses of polio and pentavalent, and measles vaccines.
[5] Socioeconomic status derived using Principal Components Analysis of household possessions
[6] Village size is the number of births in the village for 2012 calendar year

Table 6.3 Baseline characteristics of study participants enrolled in Mobile Solutions for Immunization (M-SIMU) trial using intention-to-treat analysis

	Control (N=22)		SMS (N=32)		75KSH[1] (N=27)		200KSH[1] (N=25)	
Variable	n	%	n	%	n	%	n	%
Villages	13	24.5%	14	26.4%	14	26.4%	12	22.7%
Region								
Asembo	11	50.0%	7	21.9%	4	14.8%	6	24.0%
Gem	11	50.0%	25	78.1%	23	85.2%	19	76.0%
Mother's age (yrs)[2]	27.1	1.3	25.6	1.1	24.8	1.1	22.8	1.2
Mother's education (yrs)[2]	9.4	0.6	8.3	0.4	8.5	0.5	9.0	0.5
Antenatal care visits[2]	4.4	0.4	3.5	0.2	3.2	0.3	4.0	0.4
Place of last delivery								
At home	4	18.2%	8	25.0%	12	44.4%	9	36.0%
Health Facility	18	81.8%	24	75.0%	15	55.6%	16	64.0%
Marital Status								
Single	2	9.1%	7	21.9%	6	22.2%	6	24.0%
Married/Cohabitating	20	90.9%	25	78.1%	21	77.8%	19	76.0%
Mobile phone access								
Shares phone	6	27.3%	10	31.3%	17	63.0%	15	60.0%
Owns phone	16	72.7%	22	68.8%	10	37.0%	10	40.0%
Children under 5 in house[2]	2.0	0.1	1.9	0.1	1.8	0.1	1.7	0.2
People in house[2]	4.9	0.2	4.9	0.3	5.0	0.3	4.3	0.2
Age infant enrolled (d)[2]	20.1	1.8	19.0	1.7	17.7	1.7	22.1	1.5
Maternal English Reading Literacy								
Easily	11	50.0%	13	40.6%	8	29.6%	9	36.0%
With difficulty/None	11	50.0%	19	59.4%	19	70.4%	16	64.0%
Infant's gender								
Female	10	45.5%	12	37.5%	13	48.2%	19	76.0%
Male	12	54.6%	20	62.5%	14	51.8%	6	24.0%
Travel time to clinic								
≤30 min	20	90.9%	16	50.0%	24	88.9%	18	72.0%
>30 min	2	9.1%	16	50.0%	3	11.1%	7	28.0%

Abbreviations: ITT, intention-to-treat; SMS, short message system; KSH, Kenyan Schilling; d, days

[1] 85 KSH= 1 United States Dollar as of October 2014
[2]Mean and standard errors

Table 6.4 Short message system (SMS) behavior baseline characteristics of study participants in M-SIMU using intention-to-treat analysis

Variable	Control (N=22) N	Control (N=22) %	SMS (N=32) N	SMS (N=32) %	75KSH[1] (N=27) N	75KSH[1] (N=27) %	200KSH[1] (N=25) N	200KSH[1] (N=25) %
Receives SMS weekly								
No	7	31.8%	7	21.9%	7	25.9%	9	36.0%
Yes	15	68.2%	25	78.1%	20	74.1%	16	64.0%
SMS received/ week[2]	3.3	0.4	2.6	0.2	2.7	0.2	3.3	0.3
Sends SMS weekly								
No	11	50.0%	18	56.3%	13	48.2%	9	36.0%
Yes	11	50.0%	14	47.7%	14	51.9%	16	64.0%
SMS sent/ week[2]	2.8	0.4	2.7	0.4	2.9	0.3	2.4	0.2

Abbreviations: ITT, intention-to-treat; SMS, short message system; KSH, Kenyan Schilling

[1] 85 KSH= 1 United States Dollar as of October 2014
[2]Mean and standard errors, only for those receiving or sending SMS, respectively

Table 6.5 Per protocol delivery of short message system (SMS) reminders for each vaccine by study arm

	Penta1 n (%)	**Penta2** n (%)	**Penta3** n (%)	**Penta1-3**[1] n (%)	**Measles** n (%)	**Total**[2] n (%)
SMS (n=32)	31 (96.9%)	28 (87.5%)	31 (96.9%)	27 (84.4%)	31 (96.9%)	121 (94.5%)
75 KSH[3] (n=27)	26 (96.3%)	23 (85.2%)	25 (92.6%)	22 (81.5%)	25 (92.6%)	99 (91.7%)
200 KSH[3] (n=25)	24 (96.0%)	21 (84.0%)	23 (92.0%)	20 (80.2%)	23 (92.0%)	91 (91.0%)
Total (n=84)	81 (96.4%)	72 (85.7%)	79 (94.0%)	69 (82.1%)	79 (96.0%)	311 (92.6%)

Abbreviations: Penta1, first dose of pentavalent vaccine; Penta2, second dose of pentavalent vaccine; Penta3, third dose of pentavalent vaccine; SMS, short message system; KSH, Kenyan Schilling

[1] Number of infants that received SMS reminders per protocol for all three doses of pentavalent. This is the per protocol sample for all analyses
[2] Cumulative number of doses, i.e. number of infants in study arm multiplied by the number of vaccines (4)
[3] 85 KSH= 1 United States Dollar as of October 2014

Table 6.6 Number of correct short message system (SMS) reminders delivered per protocol for infants by study arm

	4 correct n (%)	**3 correct** n (%)	**2 correct** n (%)	**1 correct** n (%)	**0 correct** n (%)
SMS (n=32)	27 (84.4%)	3 (9.4%)	2 (6.3%)	0 (0%)	0 (0%)
75 KSH[1] (n=27)	22 (81.4%)	2 (7.4%)	2 (7.4%)	1 (3.7%)	0 (0%)
200 KSH[1] (n=25)	20 (80.0%)	3 (12.0%)	0 (0%)	2 (8.0%)	0 (0%)
Total (n=84)	69 (82.1%)	8 (9.5%)	4 (4.8%)	3 (3.6%)	0 (0%)

Abbreviations: SMS, short message system; KSH, Kenyan Schilling

[1] 85 KSH= 1 United States Dollar as of October 2014

CAPTION: The column headers indicate the cumulative total of vaccine doses that received SMS reminders per protocol. For example, 3 correct indicates that for three vaccines, the SMS reminders were delivered to the mother's mobile phone both three days and one day before the scheduled date

Table 6.7 Crude and adjusted hazard ratios for pentavalent3 coverage

		Study Arm			
		Control	SMS	SMS + 75 KSH[1]	SMS + 200KSH[1]
Intention-to-treat	No. of participants[2]	22	29	27	24
	Vaccinated[2]				
	No.	21	26	24	24
	% (95% CI)	95.5 (77.1-99.9)	89.7 (72.6-97.8)	88.9 (70.8-97.6)	100 (85.8-100.0)[4]
	Unadjusted				
	HR (95% CI)	1 (Reference)	0.83 (0.48-1.44)	1.17 (0.64-2.16)	2.95 (1.69-5.16)
	P value		0.506	0.609	0.001
	Adjusted[3]				
	HR (95% CI)	1 (Reference)	1.00 (0.50-1.98)	1.15 (0.55-2.44)	3.33 (1.71-6.47)
	P value		0.994	0.708	0.001
Per protocol	No. of participants[2]	22	24	22	19
	Vaccinated[2]				
	No.	21	21	21	19
	% (95% CI)	95.5 (77.1-99.9)	87.5 (67.6-97.3)	95.5 (77.1-99.9)	100 (82.4-100.0)[4]
	Unadjusted				
	HR (95% CI)	1 (Reference)	0.74 (0.41-1.32)	1.49 (0.75-2.98)	3.23 (1.76-5.92)
	P value		0.304	0.254	0.001
	Adjusted[3]				
	HR (95% CI)	1 (Reference)	0.91 (0.41-2.03)	1.50 (0.71-3.61)	3.89 (1.88-8.02)
	P value		0.829	0.260	0.001

Abbreviations: SMS, short message system; KSH, Kenyan Schilling; HR, hazard ratio

[1] 85 KSH= 1 United States Dollar as of October 2014
[2] Pentavalent3 vaccination by 24 weeks of age in those who reached 24 weeks of age
[3] Adjusted for phone ownership, time to clinic, and region *a priori*
[4] One sided, 97.5% confidence interval

Table 6.8 Crude and adjusted hazard ratios for measles coverage

		Study Arm			
		Control	SMS	SMS + 75 KSH[1]	SMS + 200KSH[1]
Intention-to-treat	No. of participants[2]	22	28	25	24
	Vaccinated[2]				
	No.	18	20	18	23
	% (95% CI)	81.8 (59.7-94.8)	71.4 (51.3-86.8)	72.0 (50.6-87.9)	95.8 (78.9-99.9)
	Unadjusted				
	HR (95% CI)	1 (Reference)	0.81 (0.41-1.58)	0.85 (0.45-1.62)	1.57 (0.86-2.89)
	P value		0.530	0.633	0.142
	Adjusted[3]				
	HR (95% CI)	1 (Reference)	0.99 (0.49-2.02)	1.00 (0.47-2.12)	2.05 (0.95-4.41)
	P value		0.981	0.994	0.066
Per protocol	No. of participants[2]	22	27	23	22
	Vaccinated[2]				
	No.	18	19	17	21
	% (95% CI)	81.8 (59.7-94.8)	70.4 (49.8-86.2)	73.9 (51.6-89.7)	95.5 (77.1-99.9)
	Unadjusted				
	HR (95% CI)	1 (Reference)	0.78 (0.40-1.53)	0.94 (0.48-1.87)	1.56 (0.85-2.88)
	P value		0.471	0.871	0.154
	Adjusted[3]				
	HR (95% CI)	1 (Reference)	0.96 (0.47-1.95)	1.11 (0.51-2.45)	2.01 (0.95-4.26)
	P value		0.905	0.781	0.069

Abbreviations: SMS, short message system; KSH, Kenyan Schilling; HR, hazard ratio

[1] 85 KSH= 1 United States Dollar as of October 2014
[2] Measles vaccination by 10 months of age in those who reached 10 months of age
[3] Adjusted for phone ownership, time to clinic, and region *a priori*

Table 6.9 Crude and adjusted hazard ratios for pentavalent3 coverage stratified by phone ownership

Analysis Type	Study Arm	Phone Ownership				Phone Shared			
		Crude HR (95%CI)	P value	Adj HR (95%CI) [1]	P value	Crude HR (95% CI)	P value	Adj HR (95%CI) [1]	P value
Intention-to-treat	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	0.64 (0.37-1.11)	0.109	0.70 (0.34-1.44)	0.327	1.24 (0.37-4.17)	0.724	2.13 (0.64-7.07)	0.217
	75 KSH[2]	2.95 (1.47-5.93)	0.002	2.83 (1.19-6.72)	0.019	0.92 (0.33-2.55)	0.878	1.05 (0.37-3.00)	0.933
	200 KSH[2]	4.48 (2.08-9.65)	0.001	4.48 (2.05-9.75)	0.001	2.22 (0.89-5.59)	0.089	3.89 (1.22-12.4)	0.022
Per Protocol	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	0.56 (0.32-0.97)	0.039	0.55 (0.28-1.08)	0.085	1.23 (0.31-4.89)	0.771	2.67 (0.71-9.93)	0.144
	75 KSH[2]	2.90 (1.41-5.97)	0.004	3.05 (1.18-7.90)	0.021	1.21 (0.44-3.33)	0.710	1.82 (0.66-5.04)	0.248
	200 KSH[2]	5.42 (2.20-13.3)	0.001	5.58 (2.06-15.1)	0.001	2.21 (0.87-5.61)	0.094	4.93 (1.43-17.0)	0.012

Abbreviations: SMS, short message system; KSH, Kenyan Schilling; HR, hazard ratio

[1] Adjusted for region and self-reported time to clinic
[2] 85 KSH= 1 United States Dollar as of October 2014

Table 6.10 Crude and adjusted hazard ratios for pentavalent3 coverage stratified by time to clinic

Analysis Type	Study Arm	≤ 30 minutes from clinic				> 30 minutes from clinic			
		Crude HR (95% CI)	P value	Adj HR (95%CI) [1]	P value	Crude HR (95% CI)	P value	Adj HR (95%CI) [1]	P value
Intention-to-treat	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	1.21 (0.55-2.62)	0.634	1.22 (0.57-2.62)	0.613	0.20 (0.05-0.78)	0.020	0.31 (0.08-1.22)	0.096
	75 KSH[2]	1.14 (0.62-2.11)	0.666	1.05 (0.49-2.24)	0.899	1.10 (0.26-4.61)	0.901	1.37 (0.18-10.1)	0.761
	200 KSH[2]	3.60 (1.91-6.76)	0.001	3.47 (1.67-7.20)	0.001	1.12 (0.27-4.54)	0.872	1.61 (0.21-12.1)	0.646
Per Protocol	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	1.15 (0.47-2.85)	0.756	1.17 (0.50-2.75)	0.718	0.12 (0.03-0.53)	0.005	0.19 (0.04-0.93)	0.040
	75 KSH[2]	1.46 (0.73-2.91)	0.289	1.35 (0.58-3.15)	0.486	0.98 (0.24-3.92)	0.975	1.84 (0.22-15.6)	0.573
	200 KSH[2]	3.92 (1.88-8.17)	0.001	3.74 (1.62-8.63)	0.002	1.11 (0.28-4.42)	0.880	2.20 (0.27-18.1)	0.462

Abbreviations: SMS, short message system; KSH, Kenyan Schilling; HR, hazard ratio

[1]Adjusted for region and mobile phone ownership
[2] 85 KSH= 1 United States Dollar as of October 2014

Table 6.11 Crude and adjusted hazard ratios for measles coverage stratified by phone ownership

Analysis Type	Study Arm	Phone Ownership				Phone Shared			
		Crude HR (95%CI)	P value	Adj HR (95%CI) [1]	P value	Crude HR (95%CI)	P value	Adj HR (95%CI) [1]	P value
Intention-to-treat	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	0.96 (0.52-1.78)	0.906	1.10 (0.60-2.03)	0.756	0.49 (0.09-2.52)	0.391	0.68 (0.17-2.81)	0.596
	75 KSH[2]	1.65 (0.81-3.36)	0.171	1.33 (0.59-2.99)	0.490	0.41 (0.10-1.71)	0.222	0.46 (0.14-1.59)	0.221
	200 KSH[2]	2.84 (1.37-5.88)	0.005	3.02 (1.49-6.14)	0.002	0.81 (0.23-2.85)	0.745	1.20 (0.41-3.50)	0.743
Per Protocol	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	0.91 (0.50-1.68)	0.773	1.02 (0.57-1.85)	0.941	0.49 (0.10-2.52)	0.396	0.74 (0.18-2.98)	0.666
	75 KSH[2]	1.92 (0.92-4.05)	0.084	1.57 (0.59-3.61)	0.287	0.46 (0.11-1.93)	0.290	0.54 (0.16-1.75)	0.299
	200 KSH[2]	2.80 (1.34-5.88)	0.006	2.94 (1.45-5.98)	0.003	0.79 (0.22-2.78)	0.709	1.36 (0.40-4.66)	0.625

Abbreviations: SMS, short message system; KSH, Kenyan Schilling; HR, hazard ratio

[1] Adjusted for region and self-reported time to clinic
[2] 85 KSH= 1 United States Dollar as of October 2014

Table 6.12 Crude and adjusted hazard ratios for measles coverage stratified by time to clinic

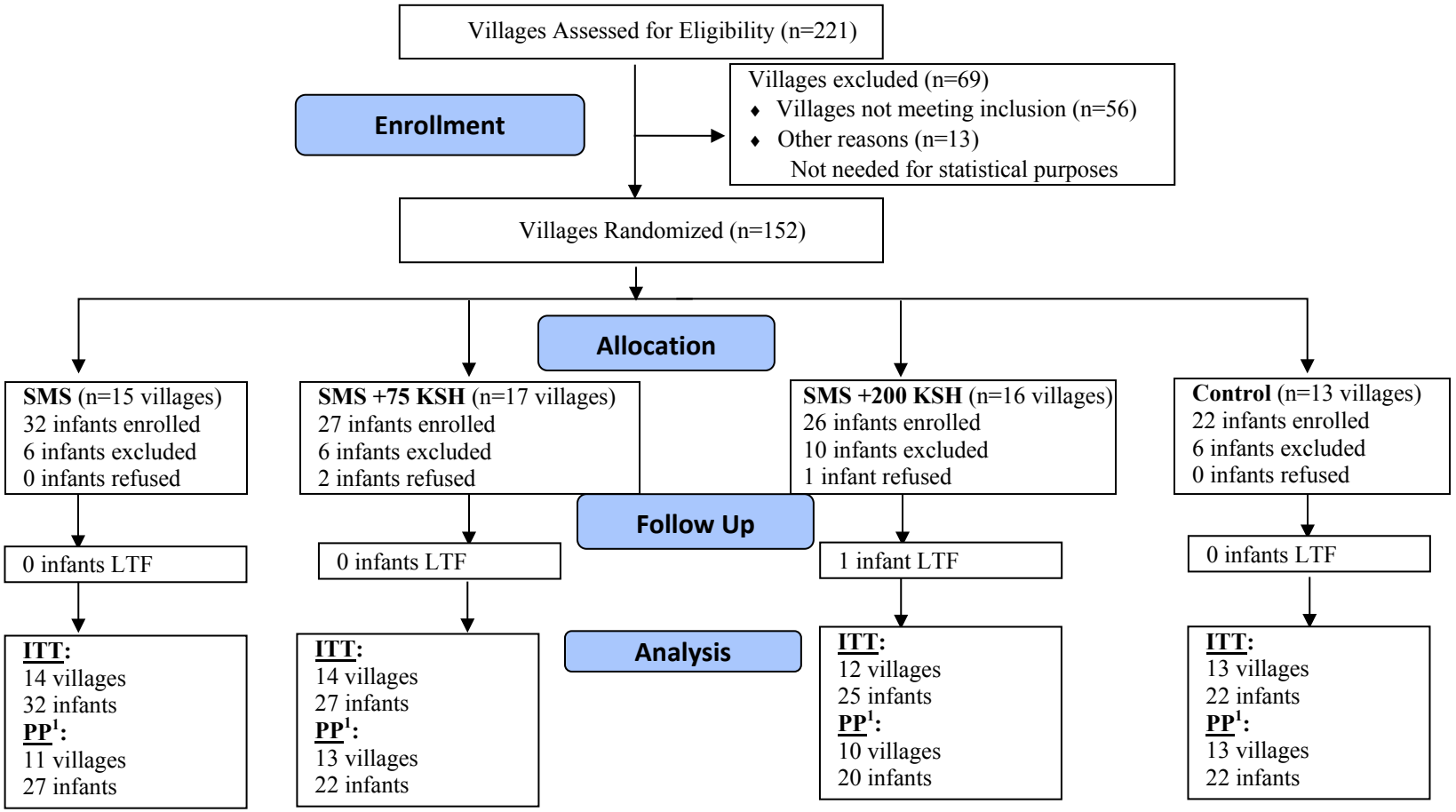
Analysis Type	Study Arm	≤ 30 minutes from clinic				> 30 minutes from clinic			
		Crude HR (95% CI)	P value	Adj HR (95%CI) [1]	P value	Crude HR (95%CI)	P value	Adj HR (95%CI) [1]	P value
Intention-to-treat	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	1.11 (0.53-2.30)	0.781	1.14 (0.53-2.43)	0.735	0.38 (0.12-1.25)	0.111	0.38 (0.10-1.51)	0.171
	75 KSH[2]	0.93 (0.48-1.78)	0.825	1.04 (0.50-2.16)	0.922	0.38 (0.09-1.69)	0.203	0.43 (0.04-4.22)	0.468
	200 KSH[2]	2.12 (1.15-3.90)	0.015	2.41 (1.11-5.23)	0.027	0.65 (0.19-2.21)	0.490	0.72 (0.07-7.25)	0.780
Per Protocol	Control	*Ref.*		*Ref.*		*Ref.*		*Ref.*	
	SMS	1.05 (0.50-2.19)	0.897	1.08 (0.50-2.31)	0.844	0.38 (0.12-1.25)	0.111	0.38 (0.10-1.51)	0.171
	75 KSH[2]	1.05 (0.52-2.15)	0.891	1.17 (0.55-2.51)	0.683	0.38 (0.09-1.69)	0.203	0.43 (0.04-4.22)	0.468
	200 KSH[2]	2.14 (1.15-3.97)	0.016	2.33 (1.10-4.97)	0.028	0.65 (0.19-2.21)	0.490	0.72 (0.07-7.25)	0.780

Abbreviations: SMS, short message system; KSH, Kenyan Schilling; HR, hazard ratio

[1] Adjusted for region, and mobile phone ownership
[2] 85 KSH= 1 United States Dollar as of October 2014

6.7 Figures for Chapter 6

Figure 6.1 CONSORT study flow diagram for M-SIMU trial



Abbreviations: SMS, short message system; KSH, Kenyan Schilling; LTF, loss-to-follow up; ITT, intent-to-treat; PP, per protocol

[1] Per protocol for pentavalent3

Figure 6.2 Short message system (SMS) and incentive delivery flow diagram

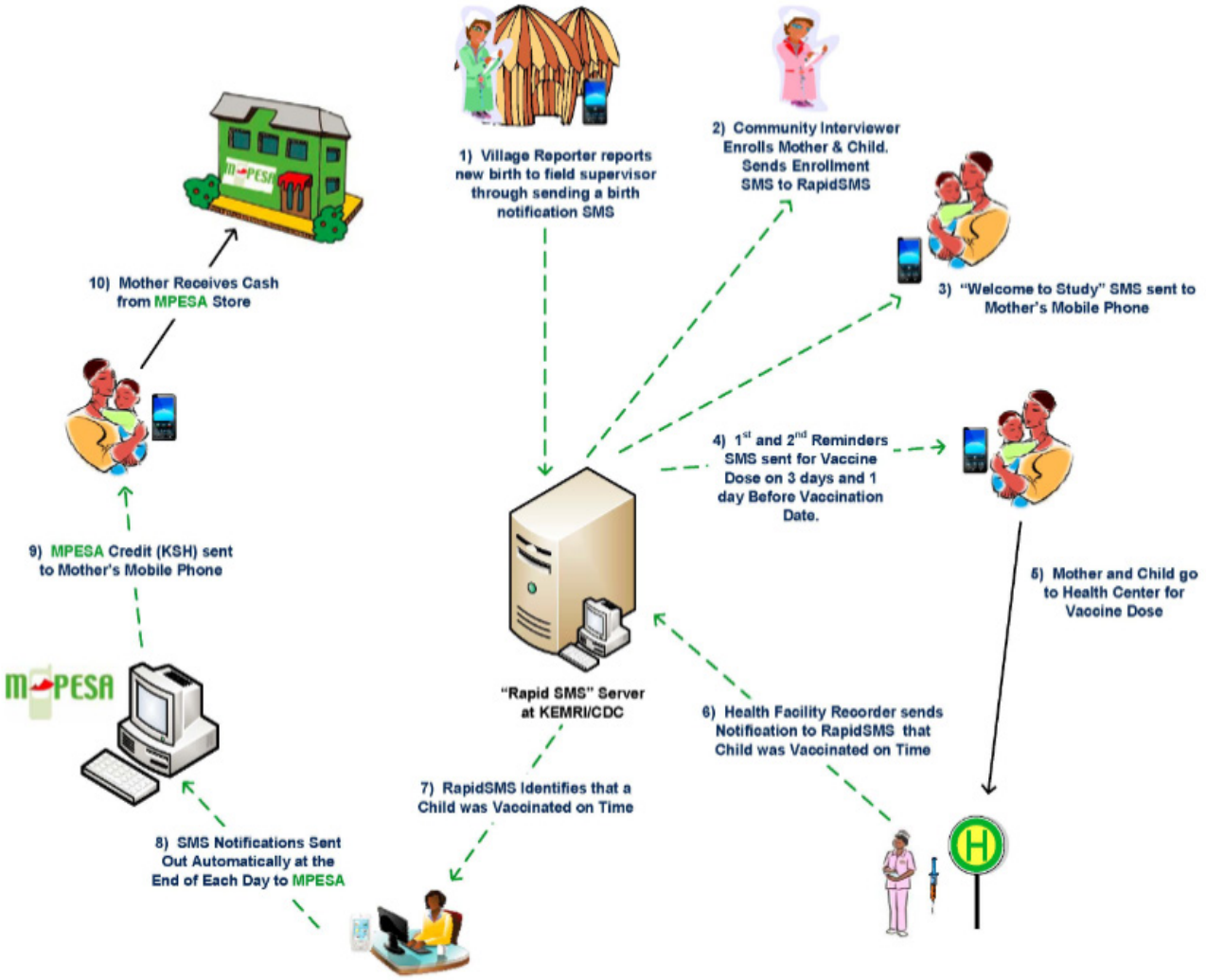
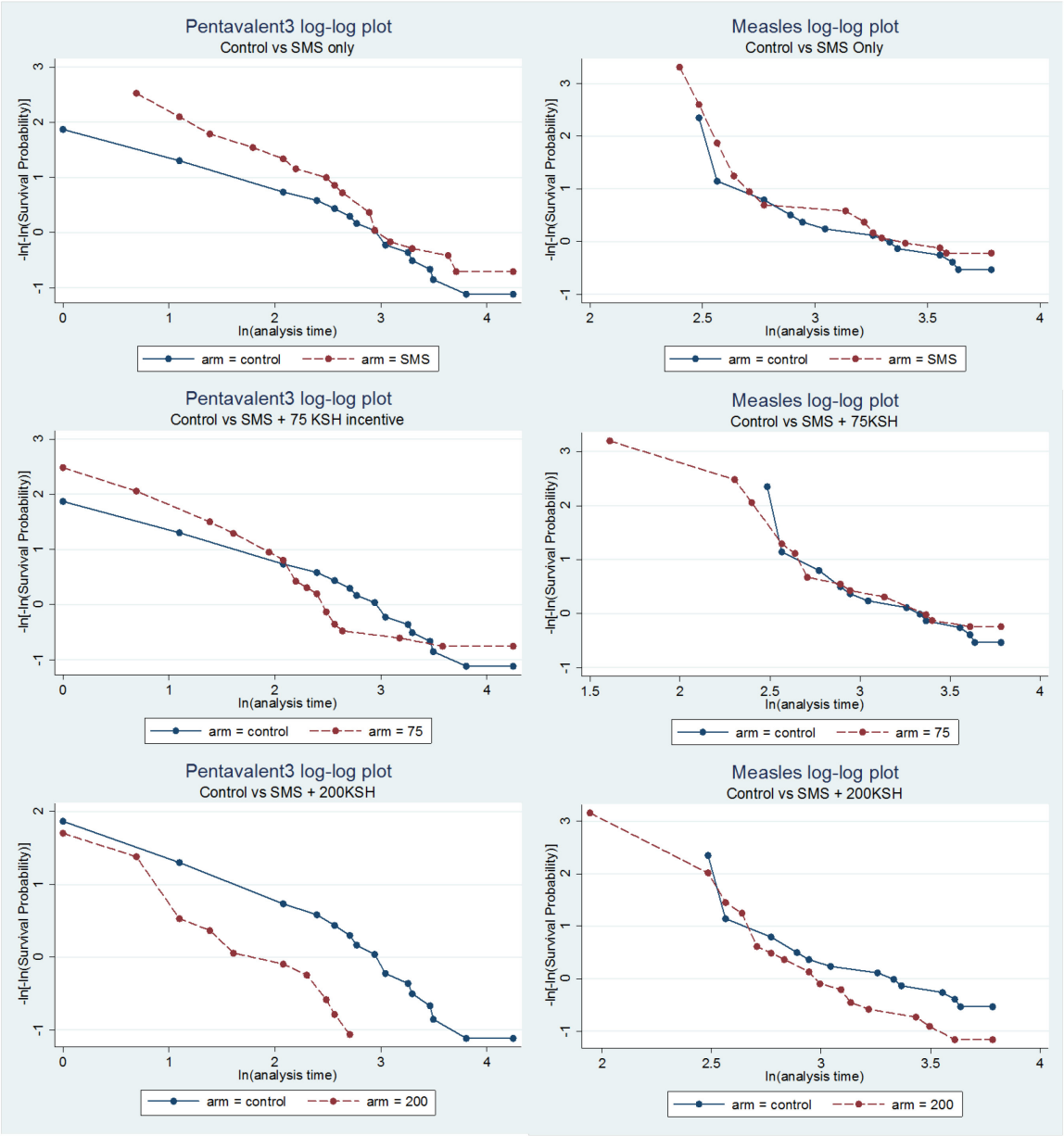


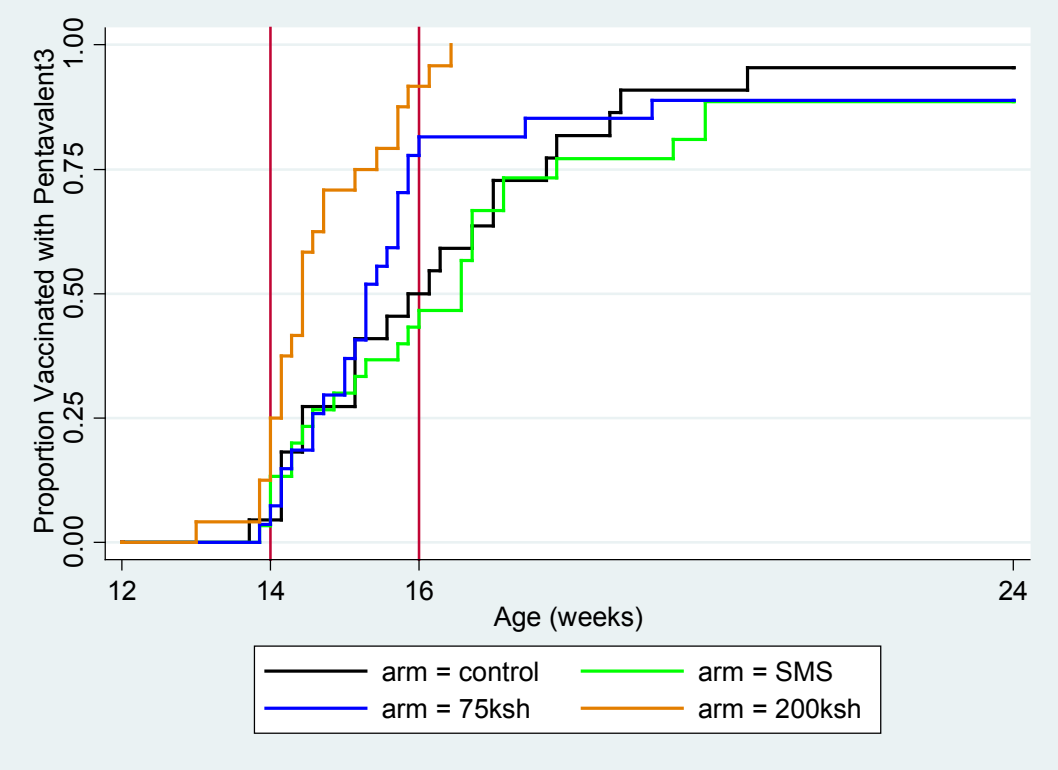
Figure 6.3 Log-log plots for proportional hazards assumption of pentavalent3 and measles vaccination



Abbreviation: KSH, Kenyan Schilling; SMS, short message system

CAPTION: For presentation purposes, analysis time was centered to 98 days and 260 days for pentavalent3 and measles vaccination

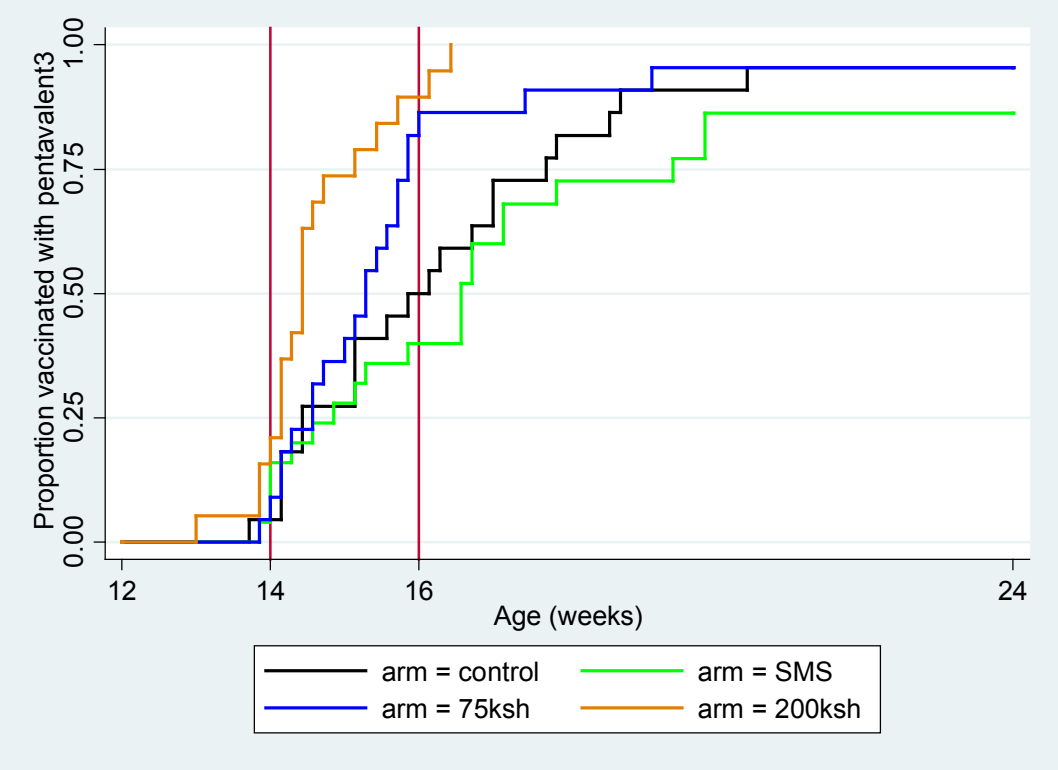
Figure 6.4 Inverse Kaplan-Meier curves for time to pentavalent3 by study arm using intention to treat delivery of short message system (SMS) reminders



Abbreviations: ITT, intention-to-treat; SMS, short message system; ksh, Kenyan Schilling

CAPTION: Infants censored at 24 weeks of age if pentavalent3 vaccine not received. Infants censored at age of death or age migrated if pentavalent3 not received and age was less than 24 weeks. Vertical reference lines at 14 and 16 weeks indicate time range that incentives are given if infants in incentive arm are vaccinated. Overall the inverse survival curves were statistically significant using log rank test for equality of curves (p=0.0001). The 200 Kenyan Schilling (ksh) curve was significantly different than the 75 ksh curve (p<0.001). There was no difference between SMS and control curves.

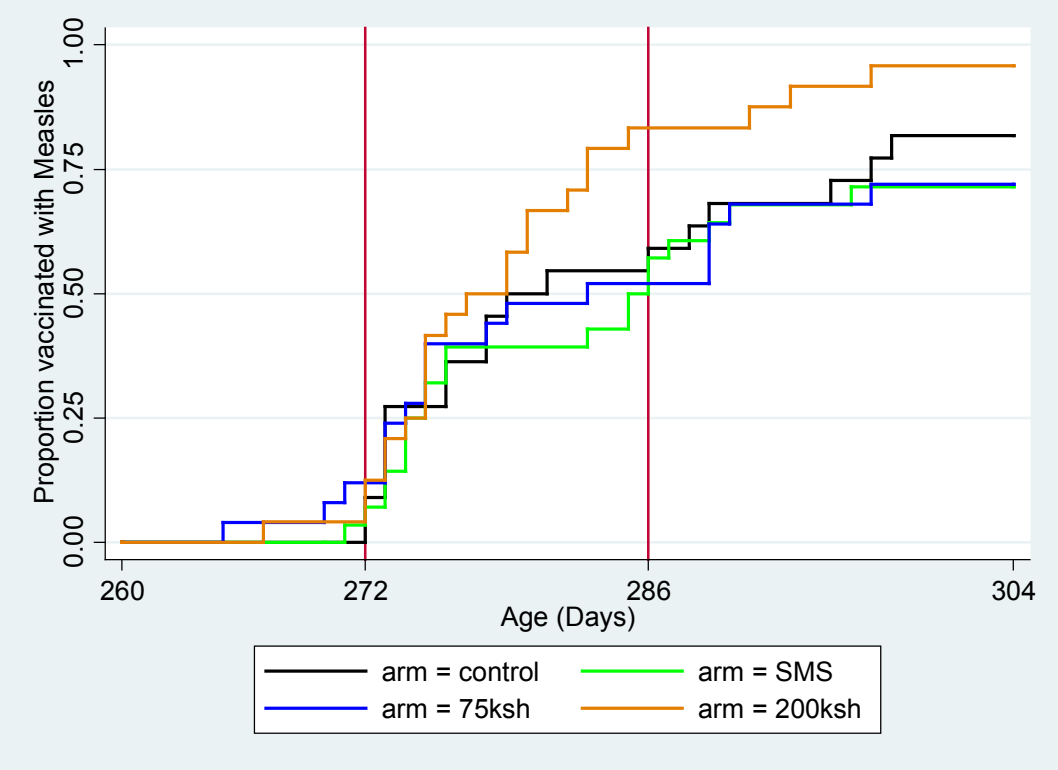
Figure 6.5 Inverse Kaplan-Meier curves for time to pentavalent3 by study arm using per protocol delivery of of short message system (SMS) reminders



Abbreviations: SMS, short message system; ksh, Kenyan Schilling

CAPTION: Infants censored at 24 weeks of age if pentavalent3 vaccine not received. Infants censored at age of death or age migrated if pentavalent3 not received and age was less than 24 weeks. Vertical reference lines at 14 and 16 weeks indicate time range that incentives are given if infants in incentive arm are vaccinated. Overall the inverse survival curves were statistically significant using log rank test for equality of curves ($p<0.01$). The 200 Kenyan Schilling (ksh) curve was significantly different than the 75 ksh curve ($p=0.03$). No difference between SMS and control curves.

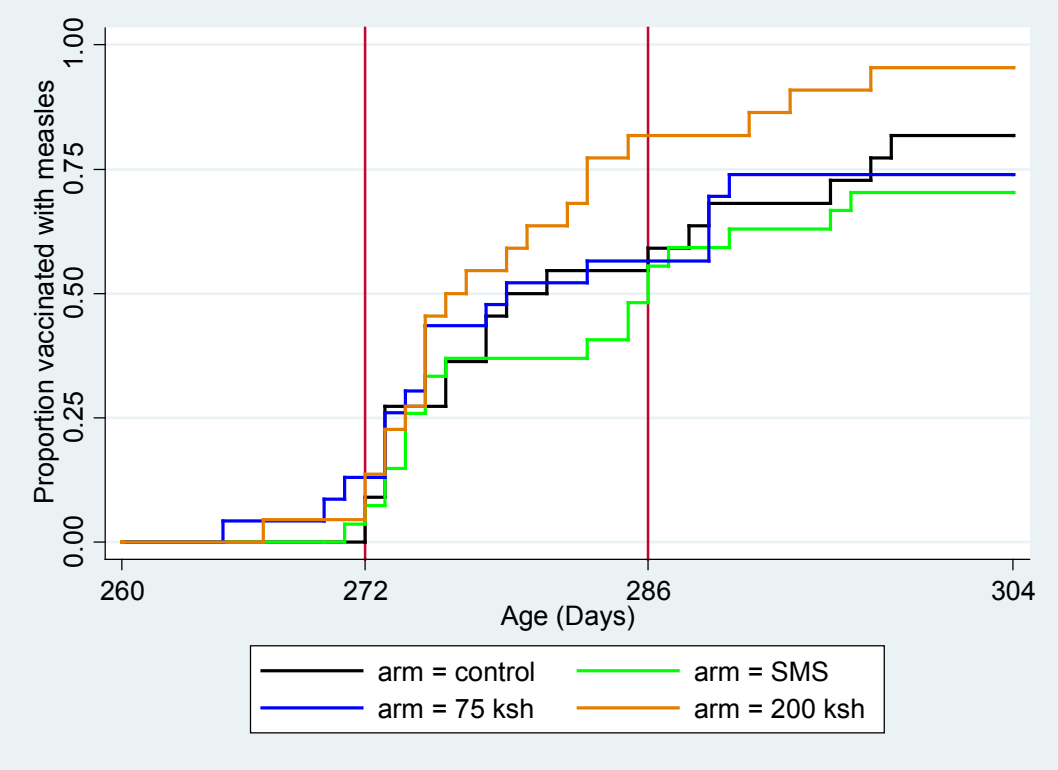
Figure 6.6 Inverse Kaplan-Meier curves for time to measles vaccination by study arm using intention to treat delivery of of short message system (SMS) reminders



Abbreviations: ITT, intention-to-treat; SMS, short message system; ksh, Kenyan Schilling

CAPTION: Infants censored at 10 months of age (304 days) if measles vaccine not received. Infants censored at age of death or age migrated if measles vaccine not received and age was less than 10 months. Vertical reference lines at 272 and 286 days indicate time range that incentives are given if infants in incentive arm are vaccinated. Overall the inverse survival curves were not statistically significant using log rank test for equality of curves (p=0.10).

Figure 6.7 Inverse Kaplan-Meier curves for time to measles vaccination by study arm using per protocol delivery of of short message system (SMS) reminders



Abbreviations: SMS, short message system; ksh, Kenyan Schilling

CAPTION: Infants censored at 10 months of age (304 days) if measles vaccine not received. Infants censored at age of death or age migrated if measles vaccine not received and age was less than 10 months. Vertical reference lines at 272 and 286 days indicate time range that incentives are given if infants in incentive arm are vaccinated. Overall the inverse survival curves were not statistically significant using log rank test for equality of curves (p=0.14).

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Chapter 7. Conclusions

This dissertation had several objectives. First, we sought to describe the study area's gaps in vaccination estimates with the implicit intention that interventions to improve timely immunization coverage are needed. Second, we assessed a rural Kenyan populations' preparedness for potential mHealth interventions by describing the epidemiology of mobile phone ownership and texting behavior while also receiving thoughts and opinions from caregivers who may receive such interventions. Lastly, we conducted a preliminary analysis of the Mobile Solutions for Immunization (M-SIMU) cluster randomized controlled trial, to determine the effect of SMS reminders with or without monetary incentives to improve timely pentavalent3 and measles immunization..

7.1 Summary of results

The key findings from the three manuscripts are presented below.

1. *Immunization coverage levels were high and consistent with previous estimates, yet a substantial proportion of infants received vaccines with delay*

We found high immunization coverage levels for routinely administered pediatric vaccines in a sample of 1746 infants with immunization card. Approximately 99.6%, 94.5%, and 83% were vaccinated for pentavalent1, pentavalent3, and measles, respectively. These estimates were similar to recent analyses conducted by others[1], and showed a marked improvement from 2003 study site estimates of vaccination coverage levels for pentavalent1 (95% coverage), pentavalent3 (68%), and measles vaccine (50%).[2] In regards to timely vaccination, similar improvements with time were observed. In 2003, proportions of timely vaccinated infants for pentavalent1, pentavalent3, and

measles were 44%, 27%, and 18%, respectively with corresponding timeliness proportion of 90%, 76%, and 71% in 2013. Measles vaccine was most likely to be delayed and also showed longest lengths of delay.

2. *Predictors for pentavalent3, measles vaccine, and FIC were similar, with delayed pentavalent1 vaccine strongly predictive of those not receiving immunizations*

Socio-demographic variables, including maternal age, maternal education, mobile phone ownership, and literacy levels, were similar for predicting both failure to receive and timely vaccinations for pentavalent3, measles, and FIC. Infants that received pentavalent1 four weeks late had highest point estimates for failure to receive pentavalent3, measles vaccine and not be fully immunized as compared to infants that received pentavalent1 on time. Sensitivity analyses that reduced definition of delay from four to two weeks found similar estimates for pentavalent3, with slight attenuations in point estimates.

3. *Caregivers think mHealth interventions offer promise for immunization, but uneven distribution of phone ownership across socio-demographic characteristics exists*

The majority of focus group participants thought that delayed immunization was still problematic in western Kenya and that mHealth-based interventions could be effective at promoting timely immunization. Participants identified several challenges with the adoption of mHealth technologies, including high levels of mobile phone sharing, phones not routinely charged, language barriers, and receiving SMS from unidentified sources. Baseline survey results found that 55% (n=1301) of mothers own a mobile phone, while 33.7% (n=794) and 4.9% (n=117) had access at the household and compound. Results from multivariate logistic regression analyses found several factors associated with

mobile phone ownership in women; these included: older age, more education, higher socioeconomic status, English literacy, and smaller household size.

Although mobile phone ownership is highly predictive of sending and receiving SMS, there is a substantial proportion of mothers who do not own mobile phones and text

Overall, 76% of mothers had received an SMS in the past week. Mothers that were married, as compared to single or divorced, and of higher socioeconomic status were associated with receiving SMS. The proportion of mothers that sent an SMS in the past week (53.5%) was lower than the proportion who received SMS. Mothers that could read English easily and were of the highest education were more likely to have sent an SMS in the past week. Although mobile phone ownership was strongly predictive of receiving and sending SMS, there were moderate levels of receiving SMS (49.7%) and sending SMS (37.4%) in mothers who do not own a mobile phone.

4. *Caregivers who were randomized to receive 200 KSH incentive ($2.25), as compared to controls, were more likely to bring infants for pentavalent3 vaccination, but not measles, with no effect observed for pentavalent3 or measles vaccine in those who were in SMS only or SMS plus 75 KSH incentive ($0.85) arms*

We found that mothers randomized to receive SMS reminders plus a 200 KSH incentive were more likely than control participants to have infants vaccinated with pentavalent3. Although statistical significance was not achieved, the higher incentive arm trended towards significance for measles vaccination (p=0.07). Mothers that received SMS reminders only or SMS reminders plus the smaller incentive were no more likely than controls to have infants vaccinated for pentavalent3 or measles.

5. *Effect modification of mobile phone ownership level on vaccination is dependent on the vaccine and intervention arm*

The significant finding of higher incentive arm infants and increased pentavalent3 vaccination did not differ by mobile phone ownership level; mothers who owned or did not own a mobile phone were both strongly associated with infant's pentavalent3 vaccination status. However, effect modification of mobile phone ownership in higher incentive arm participants was observed for measles vaccination. Caregivers that received the highest incentive and owned a mobile phone were more likely to have infants vaccinated for measles with no significant effect found in those that do not own a mobile phone..

We also found evidence for effect modification of mobile phone ownership on pentavalent3 vaccination in infants randomized to receive SMS reminders plus a 75KSH incentive; with the significant effect only observed for caregivers that owned a mobile phone. No significant findings for timely measles vaccination were found in those that received SMS plus 200KSH in either mobile phone owners or those who do not have a phone.

6. *Effect modification of travel time to clinic on vaccination is dependent on the intervention arm*

We found evidence for effect modification of travel time to clinic on pentavalent3 vaccination in infants who received SMS reminders plus 200 KSH incentive as compared to control arm infants; whereby a significant effect was observed for only infants living

less than 30 minutes from the clinic. A similar effect modification was observed for timely measles vaccination in those who received SMS plus 200 KSH incentive. We found no significant effects of SMS reminders only or SMS plus 75KSH study arms on pentavalent3 or measles vaccination in stratified analyses of time to clinic.

7.2 Implications

The results of this dissertation have implications for policies and programmatic interventions that target immunization systems and in the application of mHealth technologies in rural western Kenya and elsewhere.

1. *Recommendations for inclusion of timely and delayed immunization estimates in routine reports of immunization systems.*

In Gem District, Nyanza Province, high immunization coverage estimates were observed for the routinely administered pediatric vaccinations, yet many of the vaccines were not administered in line with the KEPI recommended schedule.[3] In higher income countries, timely vaccination estimates have been studied[4-8], with estimates of delay and timeliness recently being reported for lower-income settings.[2, 9-24] As global immunization coverage levels continually improve[25, 26], focus must shift from counting the number of children vaccinated, to counting the number of infants that are vaccinated on time and quantifying delay in vaccination. This is achievable through the inclusion of a measure of timely vaccination, where the estimate could be as simple as the proportion of infants that were vaccinated within four weeks of the scheduled date.

The inclusion of timely or delayed estimates in routine reporting systems is important for several reasons. First, delayed vaccinations lower the population's herd immunity[27],

thereby increasing the risk of exposure and possible transmission of potentially fatal pathogens. If these immunologically susceptibles are clustered, there is the potential for a vaccine-preventable disease outbreak. This is particularly important for measles vaccination, where the baseline survey indicated that only 53% of infants were vaccinated for measles by ten months of age. Measles outbreaks have occurred in settings with population immunity that reached 90%[28], which indicates how highly contagious the measles virus is.[29] Moreover, from the baseline survey, it was observed that infants vaccinated with pentavalent1 greater than four weeks from the recommend date were at greatest risk of failure to be immunized for future doses in the KEPI schedule. Although immunization timeliness and immunization coverage have traditionally been conceptualized as separate estimates, this finding highlights the interconnectedness of the two measures.

In summary, the routine reporting of immunization timeliness allows policy makers to immediately target underimmunized communities with Supplemental Immunization Activities (i.e. a measles vaccine campaign) to avert a potential outbreak. In the long term, delayed vaccination estimates can be used to identify communities with poor immunization estimates so that resources can be allocated to strengthen the routine immunization system.

2. *Recommendations to target infants with delayed pentavalent1 vaccination as a means of improving immunization coverage.*

Delayed pentavalent1 vaccination was most strongly associated with failure to be immunized for subsequent doses in a risk factor analysis of baseline data conducted in March of 2013 (n=1748). Although this finding has not been replicated in other low-

income countries, several studies conducted in the United States have also observed that infants with delayed first vaccination were at higher risk of not receiving future vaccinations.[30-33] This finding affords opportunities for programmatic interventions and policies to target this sub-population (10.2%, n=176) so that future immunizations are received.

Several interventions that can be selectively targeted to those with delayed pentavalent1 include small monetary incentives, SMS reminders, and clinic-based education of infant's caregivers. The preliminary analysis of M-SIMU, found that mother-infant pairs randomized to receive SMS reminders with a 200 KSH incentive ($2.25 USD) were more likely to receive pentavalent3 vaccination than infants who received the usual standard of care. Previous studies conducted in resource-constrained settings have shown that small incentives increased immunization rates[34, 35], HIV testing uptake[36], and adult male circumcision.[37] Although M-SIMU infants that were randomized to only receive SMS immunization appointment reminders were not significantly associated with measles or pentavalent3 vaccination, the vast majority of randomized trials conducted within sub Saharan Africa have found positive gains associated with SMS reminders across a range of different forms of health care utilization.[38-46] Lastly, clinic-based education that centers on benefits of vaccination and potential illnesses that an un-vaccinated infant could contract can be targeted to caregivers of infants with delayed first dose of pentavalent series. This approach may be more sustainable than SMS reminders or monetary incentives and has improved DTP3 completion rates in other areas.[47]

3. *Recommendations for assessment of the 'mobile phone' landscape prior to the investment of time and resources needed to bring mHealth projects to scale.*

Globally, more and more people own a mobile phone with each passing year.[48, 49] Certainly, mHealth technologies offer opportunities to advance the delivery of healthcare, improve treatment outcomes, and target the traditionally hard-to-reach populations in lower-income countries.[50, 51] With rightful optimism for mHealth as a game-changer in global efforts to reduce maternal and child mortality levels, caution and careful assessments of populations intended to receive mHealth intervention are needed before mHealth programmatic interventions are brought to scale.

Kenya is one of the leading sub Saharan African countries in mobile phone ownership levels.[52] However, a baseline survey of 2359 Kenyan mothers with infants aged 12-23 months found near uniform *access* to a mobile phone, but only 55% of mothers owned one. For interventions that target caregivers in rural Kenya, expectations for effectiveness of mHealth technologies to improve maternal and child health outcomes may need to be tempered because of the moderate level of mobile phone ownership. Moreover, mobile phone ownership was observed to be unevenly distributed across socio-demographic variables, with caregivers of higher economic status, older maternal age, higher literacy level, and higher education more likely to own a mobile phone. These socio-demographic variables were also predictive of immunization timeliness and coverage in the M-SIMU baseline survey (Chapter 4), which implies that mHealth interventions may be targeting caregivers that do not need any intervention for infant's immunization status. Similarly, stratified analyses of the M-SIMU trial found evidence that the effect of the incentive on pentavalent3 and measles vaccination was modified by

mobile phone ownership level, but studies that randomized SMS reminders for HIV treatment adherence[39] and skilled delivery found no such effect modification.[41]

In summary, although there are high levels of mobile phone sharing across Kenya, the desired effect of mHealth interventions may be contingent on whether the intended recipient owns a mobile phone. The type of mHealth intervention (treatment, monitoring, adherence, etc.) and its intended recipient (health care worker, caregiver, husband, etc.) need to be considered when implementing mHealth trials or programs.

4. *Considerations for the use of small monetary incentives to promote immunization coverage and timeliness.*

The finding that 200KSH incentives coupled with SMS reminders improved pentavalent3 vaccination rates and trended towards significance for measles vaccination, as compared to control infants, affords promise for the potential of incentives to improve timely immunization in rural western Kenya and other settings. The null finding for the 75 KSH incentive should be interpreted cautiously as the preliminary sample was underpowered to detect differences less than three-fold from the control arm.

In light of the small sample size and lack of cost-effectiveness analyses, it is prudent to not make any recommendations for wide spread use of incentives until the full M-SIMU sample is analyzed and other replication studies are conducted. However, if the present results hold true, there are several points of consideration that merit discussion. First, potential populations that would potentially benefit from incentives need to be identified. As seen in Chapter 4's immunization estimates, many mothers do not need economic incentives for immunization seeking behavior as immunization timeliness is moderate, and immunization coverage is high. Rather, and as discussed previously,

financial incentives could be targeted to caregivers of infants that present to clinic with delayed pentavalent1. This sub-population is quite small (about 10%) and these infants were found to be at higher risk for not receiving additional immunizations.

However, there is some concern that this targeted approach may have unintended consequences. By targeting infants that present with delay to clinic, financial incentives may dis-incentivize caregivers to bring their infant for vaccination. Plainly, caregivers may intentionally delay their infant's immunization in order to receive financial benefit. Rather than target sub-populations within a community and risk a de-incentivizing of vaccination, incentives could be applied uniformly in administrative regions with poor indicators of immunization. Moreover, instead of focusing on different populations, an alternative approach would be to uniformly incentivize vaccines with low coverage estimates or are given at later ages of life. Two vaccines that fit these criteria are measles and HPV vaccines. High vaccination coverage is needed to control measles transmission. If incentives improve routine delivery of measles vaccination, the need for catch-up campaigns may lessen. HPV vaccine has recently become available for the majority of Kenyan girls aged 9 to 13 years old.[53] To date, the uptake of HPV vaccine has been low; with many people unaware the vaccine is offered.[54] Additionally, the schedule for the vaccine is unlike other routine immunizations that are giving during infancy. A single national campaign that is well publicized and provided incentives for HPV vaccination could distinctly improve HPV coverage estimates in a short period of time.

5. *Recommendations to not discount future use of SMS reminders as a tool to improve immunization timeliness and coverage.*

Preliminary analyses of the M-SIMU trial found no significant effect of those randomized to receive only SMS immunization appointment reminders as compared to controls. SMS reminders have been shown to improve immunization rates in the United States[55-58] and other healthcare seeking behaviors in sub Saharan Africa.[38-46] In regards to immunizations, SMS reminders target a caregiver's forgetfulness of infant's immunization appointments or alert parents that vaccines are due if the vaccination schedule is not known. Since the present study site has high vaccination coverage and adequate levels of timeliness, and SMS reminders were not found to be effective, one could posit that forgetfulness and lack of awareness about the vaccination schedule do not explain the majority of underimmunization cases.

7.3 Strengths and limitations

This set of studies had several strengths and weaknesses. In regards to the baseline survey for immunization coverage and mobile phone ownership estimates, the sample was sufficiently large and representative. Selection bias was minimized by our attempt to survey all caregivers with infant aged 12-23 months residing within one of the 120 villages in Gem District. Moreover, we collected data on a wide range of variables that have been associated with immunization coverage and mobile phone ownership in other settings, which gives the analyses generalizability. Secondly, due to the low proportion of caregivers who provided verbal report and were excluded from analyses, our results are more protected against selection bias as compared to other studies where proportions of verbal report were much higher.[2, 22, 59] Additionally, the high proportion of caregivers with maternal and child health cards allowed for a detailed analysis of immunization timeliness. Furthermore, the risk factors obtained through the primary log-binomial

model were corroborated with multiple linear regression model that examined days delayed for each vaccine as a continuous variable. Lastly, we concurrently identified estimates of immunization coverage, immunization timeliness, and severely underimmunized, in addition to their respective risk factors, in a single sample. The majority of previous studies have typically examined either immunization coverage, or, less frequently, immunization timeliness, separately.

A particular strength of the focus group discussions was the inclusion of individual, private responses within the group setting. These responses were recorded before group discussion resumed in an attempt to minimize the effect of dominant personalities in the group discussion. Furthermore, the moderator limited the effect of dominant personalities by requesting input from each focus group discussant.

The M-SIMU cluster randomized controlled trial had several strengths that aid in the interpretation of the study results and minimized potential biases. First, we restricted our enrollment to infants that were too young to have initiated the pentavalent vaccine sequence. This enrollment strategy sought to minimize selection bias as compared to an alternative enrollment strategy where caregivers would be enrolled from the immunization clinic. Mothers enrolled from the clinic have already shown a propensity to bring their child for immunization. Since we enrolled infants before their first vaccination, we were able to capture mother-infant airs that may never go for immunization. This sub-population is important to include in our sample because it allows us to examine whether reminders, with or without monetary incentives, are effective at bringing infants to clinic for vaccination that would otherwise not be vaccinated if the interventions were absent.

A second strength of the M-SIMU trial pertains to our use of the RapidSMS system to deliver SMS reminders.[60] This is a free, open source system that has served as a platform for automated delivery of SMS reminders in other studies.[61-63] With the RapidSMS system, SMS reminders were delivered correctly for the majority of the trial's participants. Intention-to-treat-analyses (ITT) that included caregivers who did and not correctly receive SMS reminders found significant effects of SMS plus 200KSH and represent the effectiveness of the intervention.[64] Supplemental per protocol analyses found similar findings to the ITT analyses, which gives more confidence in the results.[65]

In line with the use of ITT analyses, this trial was conducted with effectiveness in mind. First, there was minimal contact with trial participants and clinic staff so as to not disrupt participant's routine care seeking behavior and clinic's routine delivery of care. Caregivers were only approached by study staff at enrollment, 12 month follow-up visit, and if caregivers brought their child for immunization, a short survey was conducted. Second, mother-caregiver pairs were enrolled independent of mobile phone ownership, which is an important consideration in light of baseline survey estimates that found only 55% of caregivers possessed a mobile phone.

This set of studies had several limitations that merit a thorough discussion. In regards to the mobile phone ownership and immunization coverage survey, a limitation is that all eligible mothers may not have been surveyed. KEMRI/CDC provided a census of all known mothers with infants aged 12-23 months old. The provided census may have contained missing households as surveillance activities in Gem District recently resumed and the mapping of households may not be complete. If these missing households were systematically different than those included in the baseline survey, the results could be

biased. If these households were in more remote locations, it is likely that the socio-demographic characteristics of its occupants were poorer than those that were identified. This would potentially cause overestimates of mobile phone ownership and timely immunization coverage.

A similar selection bias concern exists for the M-SIMU trial. Overall, 15% of infants were ineligible because they were identified after 35 days of age (Table 6.1). Approximately 10% of control and SMS only arms were excluded due to overage compared to 17% 19% of infants in SMS plus 75KSH and SMS plus 200KSH arms. If infants that were excluded due to overage were systematically different across study arms in covariates that were predictive of delayed immunization, the results may be overestimated. Of note, the high percentage of infants excluded because of overage was due to the commencement of the trial. Village reporters were asked to send SMS notifications for all births identified in the past month. The large backlog of birth notifications meant that some children had already aged to 35 days since they were first identified. Omitting preliminary analysis infants, the proportion of infants excluded due to overage in the full M-SIMU samples was approximately 3% (58 infants excluded from 1995 households visited; Data not shown).

Another avenue for selection bias in the M-SIMU trial stems from the cluster design and consequent decision to not blindly allocate participants to study arm as separate consent forms were used to enroll mothers in each of the four arms. Selection bias could be present if there was selective drop-out or refusal in those residing in control arm villages. This is less of a concern as no participants withdrew from the study and only three individuals refused (two in the 75 KSH arm and one in the 200 KSH arm).

However, since allocation was known by study staff, it is possible that there may be ascertainment bias in our collection of immunization information at the twelve month follow-up visit, where community interviewers may be more likely to mark an ambiguous vaccination date in intervention arms as timelier than controls. This would inflate our estimates of intervention effects. As discussed previously, our prospective immunization data collection from the clinic is compared to data recorded from twelve month follow-up visits. If there were differences in dates, a field investigation was made to resolve the discrepancy.

Potential selection bias may also be found in the analysis of immunization timeliness and coverage. The sample only consisted of mothers that had a written history of infant's immunization status (i.e. the maternal and child health booklet). Mothers who provided verbal report of infant's immunization history were excluded from analysis. Previous studies have found several characteristics associated with retention of immunization booklet, including but not limited to, younger infants, less people in a household, delivery at a health facility, and male infants.[66-68] If the characteristics of caregivers who provided verbal report systematically differed from those who provided written records, and those characteristics were associated with underimmunization, the estimates of immunization coverage and timeliness may be overestimated. However, the analysis of risk factors for verbal reporting, as compared to maternal child health card present at time of survey, found that female infants, households greater than two kilometers from the clinic, and older infants were associated with a caregiver's provision of verbal immunization history. Although distances to clinic and infant's gender were

not associated with any of the immunization outcomes, older infants were associated with decreased immunization coverage and increased immunization delays.

The primary purpose of the baseline survey was to obtain current estimates of immunization coverage, mobile phone ownership, and other demographic variables that were used for M-SIMU sample size and randomization. As such, our analyses may suffer from unmeasured confounding bias[69] as we did not collect a comprehensive list of socio-demographic variables that have been found to be associated with mobile phone ownership and immunization coverage in other studies. Specifically, community health worker interactions[1], antenatal care seeking behavior[19, 24], paternal demographics[9], and place of delivery[13] have been associated with immunization coverage in other studies, but were not assessed in our analyses. The omission of these variables may result in changes of point estimates and significant risk factors for immunization coverage and timeliness. In regards to the M-SIMU trial, randomization should ensure that both known and unknown covariates of timely immunization are equally distributed across study arms. Still, we conducted unadjusted and adjusted analyses to assess the effect of interventions on timely pentavalent3 and measles vaccination. Moreover, primary outcomes were stratified by mobile phone ownership and travel time to clinic to assess the potential for effect modification.

The present studies are also at risk for non-differential measurement bias which would bias results towards the null. The recording of immunization history is most likely to suffer from this bias as immunization booklets in older infants are often in poor condition; making it more difficult to accurately transcribe immunization dates. We sought to minimize this bias through the use of quality control measures preprogrammed

into data collection instruments. Moreover, we extensively cleaned immunization data prior to analysis. Questionable data points were relayed to the field team for follow-up. In the M-SIMU trial, the likelihood of measurement bias in the immunization dates is much lower than the immunization dates from the baseline immunization timeliness and coverage survey because of the prospective data collection of vaccination dates. For mobile phone ownership, participants may have indicated that they owned a mobile phone when they actually did not because of possible feelings of embarrassment. This would have led to over estimates of mobile phone ownership and an attenuation of the effect size observed for predictor variables associated with mobile phone ownership.

An additional limitation of the M-SIMU preliminary analysis is the small sample size. This cohort of enrolled mother-infant pairs was created so that the study investigators could assess the readiness of both the automated SMS delivery system and mobile phone based data collection tools; it was not designed with a statistical analysis in mind and therefore was underpowered. Power analyses found that the study had approximately 50% power to detect a hazard ratio of 2.0 in both pentavalent3 and measles vaccination primary outcomes. The results presented in this dissertation, particularly the null findings of SMS only and SMS plus 75KSH interventions should be interpreted cautiously.

In regards to our three focus group discussions, there was potential for interviewer bias. We sought to minimize this bias through the use of a semi-structured questionnaire that was used in all three groups. This questionnaire ensured that all key talking points were discussed in each group. Moreover, the focus group moderator and assistants were extensively trained in focus group techniques. Additionally, although we did not mention

to focus group participants that the FGD's purpose was to inform the M-SIMU trial, 'courtesy bias' may potentially explain the positive thoughts on mHealth interventions of our FGD.

7.4 Generalizability of results

There are some concerns about the external validity, or generalizability, of this dissertation's results that stem from the population's characteristics and the M-SIMU study design and implementation. Our baseline survey indicated high levels of immunization coverage and moderate levels of vaccination delays. This finding may impact the generalizability of several observed results. First, our finding that delayed pentavalent1 vaccination was associated with infants that did not receive pentavalent3 and measles vaccine, may only be applicable for this study site. Second, the observed null finding that infants randomized to receive only SMS reminders showed no difference in vaccination status as compared to control infants may be a study-site specific finding. With high value placed on vaccination in this community, evidenced by high immunization rates, SMS reminders may not target the major determinants of underimmunization. The use of SMS reminders to improve immunization timeliness and coverage should not be discounted for other settings.

In regards to the M-SIMU study design; there are concerns that the design and implementation of this study can only be conducted within Kenya because of its high penetration of mobile phone ownership and ubiquitous mobile money system. Therefore, this study could not be replicated in other less technologically advanced settings. However, the components of the interventions in M-SIMU can be disaggregated into individual modules (SMS reminders, incentives) and can be applied based on a country's

available technology. For example, instead of transferring cash via mobile-money, incentives can be given by providing mobile phone airtime or cash vouchers.

Lastly, the M-SIMU study was conducted within the KEMRI/CDC Health and Demographic Surveillance System. The results may not be generalizable because the community is keenly aware of KEMRI/CDC's research agenda and participate in quarterly household visits to collect socio-demographic information. Moreover, the infrastructure of KEMRI/CDC allows for early identification of newborns, which other study sites may not have.

7.5 Recommendations for future research

There are several avenues of additional research that could be pursued based on the findings and methodology of this dissertation. Several of these studies address concerns about generalizability. First, additional immunization surveys conducted in Kenya and other lower income countries should be conducted to obtain estimates of timeliness and to test whether the finding that delayed pentavalent1 vaccine predicts immunization drop-out holds true in other settings. If this finding is valid in other settings, interventions and policies could target caregivers of infants with delayed vaccination to prevent future drop-out. In regards to M-SIMU, a replication study is needed. Preferably, this study would be conducted in a setting where estimates of immunization coverage and timeliness are poorer than the present study site. In such settings, SMS reminders may show a positive effect on immunization rates.

There are several other studies that alter the M-SIMU study design to answer scientific questions not related to generalizability. First, one could conduct a study

similar to M-SIMU but instead of providing incentives for every timely vaccination, participants would have pre-established odds of receiving an incentive, such as in lottery systems. There is some evidence from behavioral economics that lottery based systems may be more effective than providing fixed incentives.[70, 71] Moreover, if a lottery system is employed, incentive amounts could be increased since participants are not being paid every dose. As found in our pilot analysis, the larger incentive was much more effective than the smaller incentive at eliciting timely immunization. Second, rather than changing incentive structure, future trials could consider providing a mobile phone as the intervention. As global awareness and efforts to improve immunization systems are at its highest levels[72-74], countries are scaling efforts to improve routine immunization reporting estimates. In the dissertation's study area, clinic nurses call some mothers whose infants have defaulted on their immunization schedule. The provision of a mobile phone may be sufficient to improve immunization rates. This trial could be designed with either efficacy or effectiveness in mind. An efficacy trial would entail training clinic staff to identify immunization defaulters and call the caregiver's mobile phone to remind them that vaccinations are overdue. An effectiveness trial would only provide the mobile phone with no clinic training. Moreover, a mobile phone only study arm could be included in other M-SIMU replications where mothers randomized to this arm receive a mobile phone but do not receive SMS reminders or incentives.

A more pragmatic approach to M-SIMU replication studies, which builds off the delayed pentavalent1 vaccine predicting immunization drop-out finding, would be to randomize infants who present to the clinic for pentavalent1 delayed to control, SMS reminders, and SMS reminders plus incentive arm for their future immunization doses.

There are several other questions surrounding incentives and SMS reminders that this dissertation did not address. Qualitative studies of enrolled caregivers would be helpful in understanding participant's perceptions on receiving SMS and incentives for immunization and how these interventions were received if participants did not own mobile phones (i.e. someone relayed them reminder messages and payments). This qualitative study would offer tremendous insight as to why SMS reminders were not effective at improving immunization timeliness and also may address some of the potential barriers if the intervention was brought to scale.

Equally important to qualitative studies, cost-effective analyses are needed prior to scalability and sustainability discussions. The calculation of intervention costs is straight forward, but the definition of benefits will require consideration. The ideal definition of benefit is a reduction in disease morbidity and mortality, but our study only captured immunization coverage. Advanced modelling could extrapolate how changes in immunization coverage reduce disease morbidity and a cost-benefit estimate for dollars per case averted calculated. An additional analysis would be to compare the cost of immunization for one child through outreach activities versus the intervention.

As discussed previously, there is some concern about a negative rebound effect associated with removal of incentives. The discontinuation of incentives might result in immunization coverage levels that were lower than baseline. Comparisons of immunization history in subsequent born infants of M-SIMU enrolled caregivers would address this concern.

Two additional studies are possible because of the high-quality, prospectively-collected immunization data in the M-SIMU trial. Immunization history is often

collected retrospectively and can be prone to multiple biases and sources of error.[75-77] The first proposed study would compare M-SIMU enrolled infant's immunization history using three data sources; the prospectively collected SMS records from M-SIMU; the 12 month M-SIMU follow-up visit; and KEMRI/CDC Health and Demographic Surveillance data that is collected every four months for infants under five years of age.

Accurate vaccination history is important for national immunization programs so that resources can be relocated to poor performing areas if needed. However, these estimates do not reflect the actual percentage of individuals that are truly protected from disease as vaccines do not produce an immunological/protective response in all individuals. Serum based assays are the gold standard to measure whether infants are immunologically protected. However, bringing these methods to scale is unrealistic because a costly and time-consuming venous blood draw is required. Instead, non-invasive collected body fluids, such as oral fluid or dry blood spots from finger pricks, could be used to test for the presence of immune-markers, which are biological correlates of an infant's immunological protection to vaccine preventable diseases.

Although the immune marker field is in its infancy, early results are promising.[78-81] As we are one of the few groups with rigorous, prospectively collected immunization data, we have been awarded a grant to develop field-friendly methods to assess effective vaccination coverage in young children for measles and tetanus vaccines. Knowing with certainty whether a vaccine was given, and if given, the precise date of immunization, is the key component needed in order to validate our dried blood spot and oral fluid samples with blood serum and to determine differences in antibody levels by number of doses received and their timing.

Lastly, additional cross-sectional surveys of mobile phone ownership and SMS behavior should be conducted. As mobile phone ownership levels continually grow in lower-income countries rapidly[48, 49], estimates become obsolete by the time they are published. Baseline levels of mobile phone ownership are important parameters to consider when implementing or scaling-up mHealth interventions.

7.6 Overall conclusions

Approximately 6.3 million children died before their fifth birthday in 2013, with many of the leading causes of death attributed to vaccine-preventable diseases.[82] Pneumonia and diarrhea accounted for about 1.5 million deaths in children under five years old, with measles, pertussis, tetanus, and meningitis, four other vaccine preventable diseases, responsible for an additional 362,000 deaths.

Since the creation of the Expanded Programme on Immunization (EPI) in 1974, there has been remarkable progress in raising global immunization coverage levels[25, 26] with subsequent gains in reductions of childhood morbidity and mortality from vaccine preventable diseases.[83, 84] Still, there are populations that neither receive all of the scheduled vaccines[85] nor receive vaccines in a timely manner.[11, 86] In rural western Kenya, we found that 99%, 95%, and 83%, of Kenyan infants received pentavalent1, pentavalent3, and measles vaccines, respectively, with delays in vaccination most likely for pentavalent3 and measles vaccines.

As mobile phone ownership becomes more common in low-income countries[48, 49], the use of mobile health tools to enhance or supplement delivery of proven interventions becomes more realistic.[51] Short message system (SMS) reminders[87-89] and incentives conditioned on completion of positive behavior[34-37] have been found to be effective for

other outcomes, but have not been rigorously studied in sub Saharan Africa until this dissertation.

In our study area, where approximately 55% of mothers own a mobile phone, but there is near uniform access to one, we conducted a village randomized controlled trial to test the efficacy of SMS reminders and monetary incentives conditioned on timely vaccination. We found that infants of caregivers who received SMS reminders plus a 200KSH incentive ($2.25) were significantly more likely to receive pentavalent3 and measles vaccines as compared to control arms, with no significant effects on primary outcomes for infants randomized to receive SMS reminders only or SMS reminders plus a 75KSH. This positive finding of $2.25 incentives hints at the potential for financial incentives and mobile phone technologies to improve timely immunization coverage estimates in resource-constrained settings.

7.7 References

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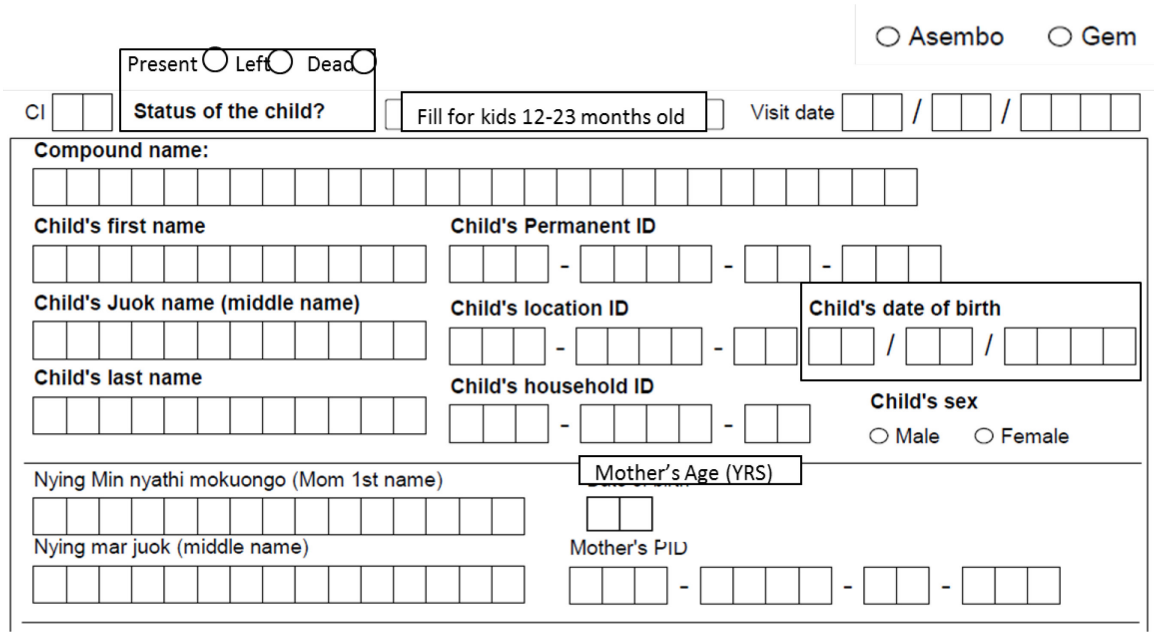
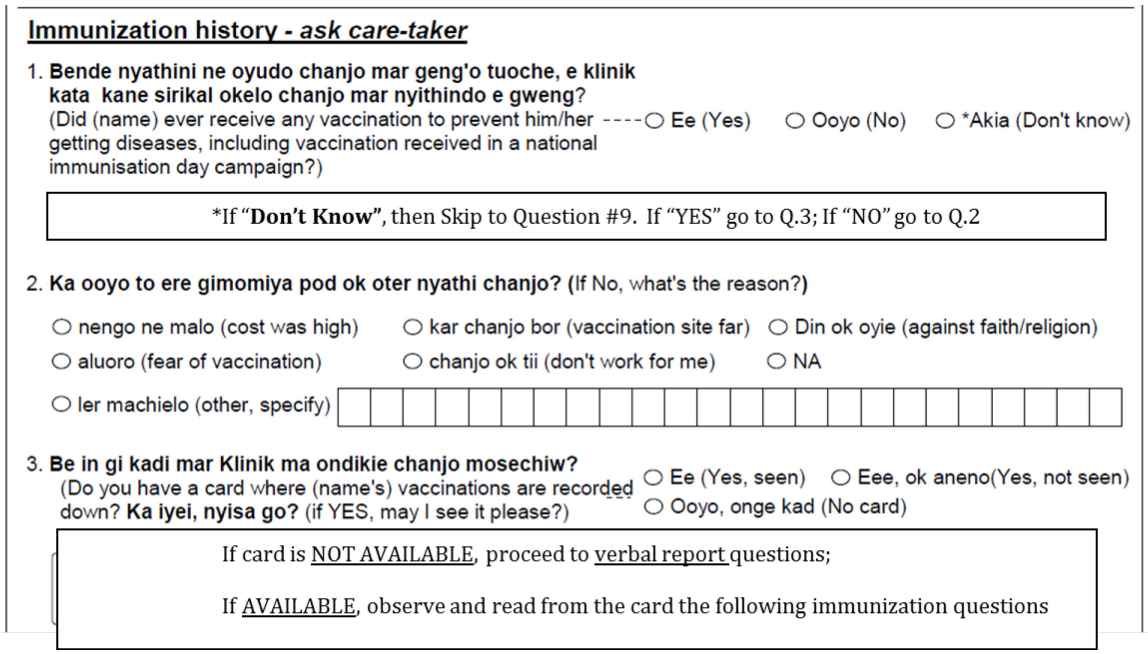
Chapter 8.

Appendix 1. Baseline survey of immunization coverage, mobile phone ownership, and demographic variables





Where card is available, fill the "FROM CARD" column Only using the information from the card in the table below. If a card is not available, obtain from the verbal report and mark "VERBAL REPORT" column

4. Complete the table below either via the information from the vaccine card or from verbal report

write in 99 in day column if card shows that a vaccination given has no date recorded or date is invalid

	FROM CARD					FROM VERBAL REPORT				
Chanjo Vaccine	**Ochiw** given	**Ok ochiw** Not given	**On which date?** **Odiochieng** Day	**/ Dwe** / Month	**/Higa** / Year	**Ochiw** Given	**Ok ochiw** Not given	**Akia** Don't Know	**Hik nyathi saa chanjo** Age at Vaccination	**Health facility where Vacc. given**
BCG Vacc. - *left fore arm, at Birth*	○ bcg1given	○ bcg1ngiven	/	/ bcg1date	20	○ bcg1vgiven	○ bcg1vngive	○ bcg1dk	Week bcg1vage	bcg1hfg
DPT/HIB/Hep B1 /PENT- *thigh - **1st dose*** *Diphtheria/Pertusis/Tetenus/Hep B/H Leunzae type B - at 6weeks*	○ pent1given	○ pen1ngiven	/	/ pent1date	20	○ pen1vgiven	○ pe1vngiven	○ pent1dkn	Week pent1vage	pent1hfg
DPT/HIB/Hep B2 *- thigh **2nd dose*** *Diphtheria/Pertusis/Tetenus/Hep B/H Leunzae type B - at 10 weeks*	○ pent2given	○ pen2ngiven	/	/ pent2date	20	○ pen2vgiven	○ pe2vngiven	○ pent2dk	Week pent2vage	pent2hfg
DPT/HIB/Hep B3 *- thigh **3rd dose*** *Diphtheria/Pertusis/Tetenus/Hep B/H Leunzae type B - at 14 weeks*	○ pent3given	○ pen3ngiven	/	/ pent3date	20	○ pen3vgiven	○ pe3vngiven	○ pent3dk	Week pent3vage	pent3hfg
POLIO 0 - *oral drops at birth, OPV 0*	○ pol0givn	○ pol0ngivn	/	/ pol0date	20	○ pol0vgivn	○ pol0vngivn	○ pol0dk	Week pol0vage	pol0hfg
POLIO 1 - *oral drops at 6 weeks OPV - 1*	○ pol1given	○ pol1ngivn	/	/ pol1date	20	○ pol1vgiven	○ pol1vngivn	○ pol1dk	Week pol1vage	pol1hfg
POLIO 2 - *oral drops at 10 weeks, OPV - 2*	○ pol2givn	○ pol2ngivn	/	/ pol2date	20	○ pol2vgivn	○ pol2vngivn	○ pol2dk	Week pol2vage	pol2hfg
POLIO 3 - *oral drops at 14 weeks, OPV - 3*	○ pol3givn	○ pol3ngivn	/	/ pol3date	20	○ pol3vgivn	○ pol3vngivn	○ pol3dk	Week pol3vage	pol3hfg
Measles Vacc. - *right upper arm, at 9 months*	○ measgiven	○ measngiven	/	/ measdate	20	○ measvgiven	○ meavngiven	○ measdk	Month measvage	meashfg
Pneumococcal *- thigh - **1st dose** - at 6weeks*	○ pne1given	○ pn1ngiven	/	/ pne1date	20	○ pne1vgiven	○ pn1vngiven	○ pne1dkn	Week pne1vage	pne1hfg
Pneumococcal *- thigh **2nd dose** - at 10 weeks*	○ pne2given	○ pn2ngiven	/	/ pne2date	20	○ pne2vgiven	○ pn2vngiven	○ pne2dk	Week pne2vage	pne2hfg
Pneumococcal *- thigh **3rd dose** - at 14 weeks*	○ pne3given	○ pn3ngiven	/	/ pne3date	20	○ pne3vgiven	○ pn3vngiven	○ pne3dk	Week pne3vage	pne3hfg

5. *Vas there an error in* **Q4.?** ---------- ○ Kamano/Ee (Yes) ○ Ooyo (No) *error_q6*

6. **in which clinic was vaccines given?**

Use the key below for numbers against the health facilities, where the child got the vaccinations mentioned above, to fill in the table above, where applicable.

● 01. Abhidha ● 02. Lwak Mission ● 03. Mahaya ● 04. Ongielo ● 05. Saradiddi ● 06. Nyagoko

● 07. Ndori ● 08. Akala ● 09. Aluor ● 10. Njejra ● 11. Rera ● 12. Nyawara

● 13. Uriri ● 14. Bondo District Hospital ● 15. Madiany Sub District Hospital ● 16. Matangwe Hospial

● 17. Siaya District Hospital ● 18. Yala Sub District Hospital ● 19. Nyanza Provincial Hospital (Russia)

● 20. Kisumu District Hospital ● 21. Bar-Olengo ● 22. Ting'-Wang'i ● 23. K'otieno ● 24. Ng'iya Mission

● 26. Mamoko/Other (Ier/specify) 1. vaxwhother [ ] ● 25. Nyathengo ● 27. UNK

● 28. Mamoko/Other (Ier/specify) 2. vaxwhothe2 [ ] ● 29. Obaga

● 30. Masala ● 31. Asayi ● 32. Gongo ● 33. Masogo ● 34. Ogero ● 35. Sirembe

● 36. Wagai ● 37. Kogelo ● 38. Bar Agulu ● 39. Mulaha

7. **Nyathi ne oyudo dos mar Vitamin A?** *(Did <name> receive a Vitamin A dose, like this one (show example) during the last 6 months?* VitA

○ Kamano/Ee (Yes) ○ Ooyo (No) ○ NA ○ DK

8. **Bende nyathini ne oyudo chanjo mar alura/ang'iew kane sirikal okelo chanjo mar nyithindo e gweng'?** *(Did your child receive the measles vaccine during a measles vaccination campaign?)*

○ Ee, tarik? (Yes, date?) [ ][ ] / [ ][ ] / campdate [ ][ ][ ][ ] ○ Ooyo (No) ○ Akia (Don't know) Meascamp

9. What is the **most** important income-generating activity of the household administrator?

○ Subsistence farming ○ Fishing
○ Commercial farming ○ Housewife
○ Salaried worker (eg. teacher, nurse, office) ○ Not working
○ Small business (eg. sell maize)
○ Business owner (eg. duka, kiosk)
○ Skilled labor (eg. carpenter, tailor, jua kali)
○ Unskilled labor (eg. shamba, construction)
○ Other, Specify:

[ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ]

10. What is the **most** important income-generating activity of the spouse?

○ Subsistence farming ○ Fishing
○ Commercial farming ○ Housewife
○ Salaried worker (eg. teacher, nurse, office) ○ Not working
○ Small business (eg. sell maize) ○ NA
○ Business owner (eg. duka, kiosk)
○ Skilled labor (eg. carpenter, tailor, jua kali)
○ Unskilled labor (eg. shamba, construction)
○ Other, Specify:

[ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ]

11. What is the **main source of drinking** water for your household?

○ Lake ○ Unprotected spring ○ Stream /River ○ Borehole/well ○ Pipe in compound

○ Pond ○ Protected spring ○ Rainfall ○ Pipe in dwelling ○ Public tap ○ Other

12. hat do you do to this water before you drink it? ○ Untreated ○ Boiled ○ Chlorine ○ Alum ○ Alum&Chlorine ○ Filtered ○ Filtered&Boiled ○ Filtered&Alum ○ Boiled&Alum ○ Other

13. hat is the **primary** source of fuel for cooking in your household in the **past month**? ○ Paraffin stove ○ Charcoal ○ Gas cooker ○ Firewood ○ Other

14. **ivestock ownership *(includes ownership inside and outside study area)***

How many of each type of livestock does your household own at the moment? *If none, write and shade "000".*

	Goats	Cattle	Sheep	Poultry	Donkey	Pigs
	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐☐
0	○○○	○○○	○○○	○○○	○○	○○
1	○○○	○○○	○○○	○○○	○○	○○
2	○○○	○○○	○○○	○○○	○○	○○
3	○○○	○○○	○○○	○○○	○○	○○
4	○○○	○○○	○○○	○○○	○○	○○
5	○○○	○○○	○○○	○○○	○○	○○
6	○○○	○○○	○○○	○○○	○○	○○
7	○○○	○○○	○○○	○○○	○○	○○
8	○○○	○○○	○○○	○○○	○○	○○
9	○○○	○○○	○○○	○○○	○○	○○

15. **Other items of ownership *(includes ownership inside and outside study area)***

How many of each of the following items does your household own at the moment? *If none, write and shade "000".*

	Plough	[mattress Foam	Spring	Straw]	Cell phone	Radio	Bicycle	Sofa	Lantern	TV
	☐☐	☐☐	☐☐	☐☐	☐☐	☐☐	☐☐	☐☐	☐☐	☐☐
0	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
1	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
2	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
3	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
4	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
5	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
6	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
7	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
8	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○
9	○○	○○	○○	○○	○○	○○	○○	○○	○○	○○

SECTION 2. **Religion** *(FOR ALL)* (For mother/caregiver of infant 12-23 months)

Which Religious group do you/name belong to? ○ Catholic ○ Legio Maria ○ Roho ○ Anglican ○ Baptist ○ Methodist ○ SDA ○ Presbyterian ○ Muslim ○ Traditionalist ○ Nomiah ○ No Religion ○ No response/Don't know ○ other (specify) [ ]

SECTION 4. **Marital status:** **Of Mother: Where individual is less than 15 years old, Fill N/A for Q. 1&2**

1. What is your/name current marital status? ○ Single ○ Married/cohabiting ○ Divorce/separated ○ Widowed ○ Don't know ○ N/A
2. *(Ask either sexes)* If currently married/cohabiting, what type of marriage are you/name in? ---------- ○ Monogamous ○ Polygamous ○ Don't know ○ N/A

FOR MOTHER/CAREGIVER OF INFANT 12-23 months old, If mother not alive fill education for caregiver

Mother alive? ○ Y ○ N

Level of Education	Class/Form/YR	YRS of Education	English: Read	Write	Speak	R
○ None	[ ]	[ ][ ]	Easily:	○	○	○
○ Primary	0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○	0 ○○ 1 ○○ 2 ○○ 3 ○○ 4 ○○ 5 ○○ 6 ○○ 7 ○○ 8 ○○ ○○	With difficulty:	○	○	○
○ Sec			Not at all:	○	○	○
○ Post-Sec						

Level of edu= highest level attempted
Class/form/year= highest attempted

: Y=yes; N=no; **Sec**=Secondary sch.; **Post-sec**=post-secondary

FOR Father OF INFANT 12-23 mos old

Father alive? ○ Y ○ N ○ DK Father's Age (YRS) [ ][ ] /

Level of Education	Class/Form/YR	YRS of Education	English: Read	Write	Speak
○ None	[ ]	[ ][ ]	Easily:	○	○	○
○ Primary	0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○	0 ○○ 1 ○○ 2 ○○ 3 ○○ 4 ○○ 5 ○○ 6 ○○ 7 ○○ 8 ○○ 9 ○○	With difficulty:	○	○	○
○ Sec			Not at all:	○	○	○
○ Post-Sec						

Level of edu= highest level attempted
Class/form/year= highest attempted

=no; **Sec**=Secondary sch.; **Post-sec**=post-secondary

15. **Other items of ownership** ***(includes ownership inside and outside study area)***

How many of each of the following items does your household own at the moment? *If none, write and shade "000".*

Plough	[mattress: Foam	Spring	Straw]	Cell phone	Radio	Bicycle	Sofa	Lantern	TV
[ ][ ]	[ ][ ]	[ ][ ]	[ ][ ]	[ ][ ]	[ ][ ]	[ ][ ]	[ ][ ]	[ ][ ]	[ ][ ]
0 ○○	0 ○○	○○	○○	0 ○○	0 ○○	0 ○○	0 ○○	0 ○○	0 ○○
1 ○○	1 ○○	○○	○○	1 ○○	1 ○○	1 ○○	1 ○○	1 ○○	1 ○○
2 ○○	2 ○○	○○	○○	2 ○○	2 ○○	2 ○○	2 ○○	2 ○○	2 ○○
3 ○○	3 ○○	○○	○○	3 ○○	3 ○○	3 ○○	3 ○○	3 ○○	3 ○○
4 ○○	4 ○○	○○	○○	4 ○○	4 ○○	4 ○○	4 ○○	4 ○○	4 ○○
5 ○○	5 ○○	○○	○○	5 ○○	5 ○○	5 ○○	5 ○○	5 ○○	5 ○○
6 ○○	6 ○○	○○	○○	6 ○○	6 ○○	6 ○○	6 ○○	6 ○○	6 ○○
7 ○○	7 ○○	○○	○○	7 ○○	7 ○○	7 ○○	7 ○○	7 ○○	7 ○○
8 ○○	8 ○○	○○	○○	8 ○○	8 ○○	8 ○○	8 ○○	8 ○○	8 ○○
9 ○○	9 ○○	○○	○○	9 ○○	9 ○○	9 ○○	9 ○○	9 ○○	9 ○○

16. How many CHILDREN UNDER 5 YRS of AGE, slept in this house last night?

[__][__]

17. How many persons are sleeping in the household regularly?

(Includes children under 5) [___][___]

18. Does the mother of the infant own a mobile phone? YES….NO

If no to 18,

18.1 Does someone in your household own a mobile phone? YES…NO

If no to 18.1,

18.2 Does someone in your compound own a mobile phone? YES…NO

Appendix 2. Focus Group discussion individual survey

1.1. Age of mother (YEARS……..[____|____]

1.2. Mother's highest level of edu attempted?NONE……PRIM….SEC….POST-SEC

1.3. Mother's highest class/form/year attempted (Circle One)…1…..2…..3…..4….5….6…..7…..8

1.4. Number of mother's previous pregnancies ……. [ ]

1.5. Do you own a mobile phone (Circle One)……YES……NO…. ***If Yes, go to 1.6***

1.5.1 Does someone in household own a mobile phone you could use? (Circle One)……..YES…….NO ***If Yes, go to 1.6***

1.5.2 Does someone in compound own a mobile phone you could use? (Circle One)…YES…..NO

1.6 Did you bring a mobile phone with you today?..YES….NO…

If No, go to 1.7

1.6.1 How much credit/airtime is on the phone? [ ][ ][ ]KSH

1.6.2 How much battery charge is on the phone?..

0-25%....26-50%.....51-75%....76-100%

1.7 Password_____ Is this correct? YES….NO

1.8. Send mother a text message---"How are you today?"-

Can she open and read the text message? (Circle one) ……

YES, EASILY……YES, WITH DIFFICULTY…….NO

1.8 Top 3 Sayings for SMS in Rank Order (1=First, 3=Third)

1. [ ] [ ] **2.** [ ] [ ] **3.** [ ] [ ]

1.8.1. Other sayings? _____

_____

Appendix 3. Focus group Semi-structured questionnaire guide

1. In this area about 3 out of every 10 mothers do not get their children vaccinated. What do you think are the biggest reasons why mothers do not bring their kids for immunization?

[*If no responses, prompt with religion/forgetfulness/money/distance from clinic*]

[***After a reason is brought up, ask group how much they agree or disagree with the reason as a barrier. Hand out blank pieces of paper and have participants mark 1= strongly disagree 2=somewhat disagree 3= no feeling/neutral 4=somewhat agree 5= strongly agree***

2. What do you think are the biggest reasons why mothers might not bring their kids on time for immunization? Do you think these reasons are the same as the reasons for children not receiving any vaccinations?

[*Explain timeliness in relation to EPI schedule*]

a. Do you think clinics and health facility staff are doing a good job about reminding children for immunizations? Could this be improved?

3. We are thinking about using SMS reminders to notify mothers when children's vaccinations are used. If SMS messages were used to send immunization appointment reminders, how should the messages be worded? What components would be necessary?

[*Prompt with names? Dates? Location? What about Motivational/ Informational/ Humorous/ proverbs] [Recorders note key areas brought up]*

4. We will now give you 1 example SMS message. [pass out piece of paper with **Please bring baby Thomas for vaccination in 3 days at the nearest clinic**] Please open the message and read it. The aim of the message is to remind Mama Thomas that Thomas is supposed to receive a vaccination soon and to encourage Mama Thomas to bring Thomas in for his vaccination. What are some ways the message could be improved so as to ensure that Mama Thomas understands the message and also to encourage Mama Tom to bring Tom in for his vaccinations?

[*Discuss that we need to consider the SMS message limit – for Safaricom it is 160 characters per message. The 'template' message is 74 characters. If the message is longer than 160 characters, the message will be broken up] [RECORDERS: WRITE DOWN KEY TOPICS]*

5. We will now give you pieces of paper with the top 5 phrases from our individual conversations that could be placed at the end of the SMS message. Select the message that you think will be the most effective at getting mothers to bring their child for immunization and place it in BIN 1. Select the second most effective SMS and place it in BIN 2. Select the third most effective SMS and place it in BIN 3.

[*Provide Mother's cutouts of each SMS message…SEE NEXT PAGE FOR SMS MESSAGES-PHRASES*] [*Tally results in front of mothers*]

a. Do you think adding these phrases would be helpful?

b. Why did you pick that phrase? *[RECORDERS: WRITE DOWN KEY TOPICS]*

c. Which type of phrase would you prefer? Motivational? Religious? Humorous? Informational

d. Are there any phrases you really do not like?

e. Do you have any other phrases you think mothers would appreciate?

f. Do you think most mothers would like getting reminders about their child's immunization appointments?

g. Do you think you would like getting reminders about your child's immunization appointments?

h. What do you think some of the problems would be in sending SMS reminders? [*Any problems with Mothers who do not have mobile phones and receiving SMS messages?]*

6. [*Follow up for when mothers say phone ownership]* Do you think the message should be phrased differently for those that rely on getting messages from someone else's phone

7. We will now give you 5 pieces of paper with different numbers on them (0-Day of immunization, 1 Day before immunization, 2-3 days before, 4-6 days before, 7 days before). These are the days before an immunization visit that SMS reminder messages could be sent. Place the piece of paper that you think has the time range that will be most effective at prompting mothers to bring their child for immunization in BIN 1

[*Tally results in front of mothers*]

a. What was your reasoning for this timing? [*If needed, is there too early of a time and why, is there too late of a time and if so, why]*

8. Imagine that Mama Thomas had been told by the community health worker/nurse/clinical officer/doctor that she should take Thomas to the clinic for vaccination today. But today Mama Thomas has other work to do such as washing clothes, going to the market and cooking. We will now ask you about motivating Mama Thomas by giving her different amounts of money only if she brings baby Thomas to the clinic. For each amount, write yes or no to the question, would this amount motivate Mama Thomas. ***[The order is 100ksh, 25, 200,50, 125, 10, 75, 150, 175]***

[*Tally results in front of mothers*]

a. Did everyone pick an amount that would motivate Mama Thomas? Why did you choose that amount of money as the tipping point? Is there an amount of money that is too high?

b. Do you think providing a small amount of money (50 ksh) to mothers would be helpful to get more children immunized [*Clarify money would be sent after the mother attends the clinic]*.

c. What do you think some of the problems would be with providing mothers a small amount of money for vaccination?

9. On a scale of 1 to 5, how helpful do you think the following would be to get more children immunized where 1 is not at all helpful and 5 is very helpful *[Have mothers respond individually on piece of paper for each] 1.* **SMS messages reminding mother of the immunization date**, **2. Giving mothers 100 Ksh after she brings her child for immunization**, **and 3. SMS messages and 100 KSH**

a. Why did you choose that answer?
b. What are advantages? What are disadvantages?

Appendix 4. Ethical Approval Documentation

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840-00200, NAIROBI, Kenya
Tel (254) (020) 2722541, 2719349, 0722-205901, 0733-400003; Fax: (254) (020) 2720090
E-mail: director@kemri.org Info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1 **20th MARCH 2013**

TO: **DANIEL FEIKIN**
PRINCIPAL INVESTIGATOR

THROUGH **DR. JOHN VULULE**
THE DIRECTOR, CGHR
KISUMU

28/3/2013

FORWARDED
DIRECTOR

Dear Sir,

RE: SSC NO. 2409 - (REVISION): RANDOMIZED CONTROLLED TRIAL OF THE IMPACT OF MOBILE PHONE DELIVERED REMINDERS AND TRAVEL SUBSIDIES TO IMPROVE CHILDHOOD IMMUNIZATION COVERAGE RATES AND TIMELINESS IN WESTERN KENYA.

This is to inform you that during the 213th meeting of the KEMRI/ERC held on 19th March 2013, the above referenced study was reviewed.

The Committee concluded that due consideration has been given to the ethical issues that may arise from the conduct of the study and granted approval for implementation effective the **19th February 2013**

Please note that the authorization to conduct this study will automatically expire on **18th March 2014.** If you plan to continue with the study beyond this date please submit an application for continuation approval to the ERC secretariat by **3rd February 2014**

Any unanticipated problems resulting from the implementation of this protocol should be brought to the attention of the ERC. You are also required to submit any proposed changes to this protocol to the SSC and ERC prior to initiation and advise the ERC when the study is completed or discontinued.

You may embark on the study.

Sincerely,

EAB

DR. ELIZABETH BUKUSI,
ACTING SECRETARY,
KEMRI ETHICS REVIEW COMMITTEE

Appendix 5. Johns Hopkins University letter of reliance on Kenya Medical Research Institute (KEMRI) Ethical Review Committee

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840-00200, NAIROBI, Kenya
Tel (254) (020) 2722541, 2713349, 0722 205901, 0733-400003; Fax (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1 **May 23, 2013**

FORWARDED
DIRECTOR
CENTRE FOR GLOBAL HEALTH RESEARCH

TO: **DR. DANIEL R. FEIKIN**
(CO-PRINCIPAL INVESTIGATOR)
JOHNS HOPKINS BLOOMBERG SCHOOL OF PH AND CDC
855 N. WOLFE ST. SUITE 600, RANGOS BLDG.
BALTIMORE, MD 21205

Dear Sir,

RE: **SSC PROTOCOL NO. 2409 (REQUEST TO UTILIZE KEMRI/ERC FOR REVIEW): RANDOMIZED CONTROLLED TRIAL OF THE IMPACT OF MOBILE PHONE DELIVERED REMINDERS AND TRAVEL SUBSIDIES TO IMPROVE CHILDHOOD IMMUNIZATION COVERAGE RATES AND TIMELINESS IN WESTERN KENYA**

This is to inform you that during the 215th meeting of the KEMRI/ERC held on 21st May 2013, the above referenced notification was reviewed. The committee noted JHSPH'S request for reliance on KEMRI ERC for the above mentioned protocol.

We are glad to offer our support in your research. The Authorization Agreement will be duly signed and returned it to the address provided.

Thank you for the notification.

Yours faithfully,

EAB

DR. ELIZABETH BUKUSI,
ACTING SECRETARY,
KEMRI ETHICS REVIEW COMMITTEE

Appendix 6. Informed consent forms for focus group discussion

KEMRI/CDC AND JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

Study Title: Randomized Controlled Trial of the Impact of Mobile Phone Delivered Reminders and Travel Subsidies to Improve Childhood Immunization Coverage Rates and Timeliness in western Kenya

Investigators: Daniel Feikin, Principal Investigator, Johns Hopkins School of Public Health/International Vaccine Access Center; CDC/National Center of Emerging and Zoonotic Infectious Diseases; Frank Odhiambo, KEMRI/CDC; Benard Ochieng, KEMRI/CDC; Dustin Gibson, Johns Hopkins School of Public Health/International Vaccine Access Center; David Obor, KEMRI/CDC; Danet Opot, KEMRI/CDC; Kayla Laserson, Center for Disease Control and Prevention; Amanda Glassman, Center for Global Development; Andrew Zeitlin, Georgetown Public Policy Institute and Center for Global Development, Dagna Constenla, Johns Hopkins School of Public Health/International Vaccine Access Center; Orin Levine, Bill and Melinda Gates Foundation; Tabu Collins, Kenya Ministry of Public Health and Sanitation, Division of Vaccines and Immunizations.

Study Location: Siaya County and neighboring villages

PI Version Date: 11 February 2013

English language version

Introduction

My name is <insert name> and I am working with researchers from KEMRI/CDC and Johns Hopkins School of Public Heath, USA. I am going to give you information and invite you to be in some research. If there is anything you do not understand please ask me to stop and I will take time to explain.

Purpose of the research

This study is trying to figure out if we can use mobile phones to get more children vaccinated. We are asking you to give your thoughts on this topic along with SMS messages and mobile-money.

We will have 3 discussion groups with women and village reporters within the KEMRI/CDC HDSS area, where we plan to do a study of this subject. Each discussion group will include between 8 and 10 people.

Description of the research

We are asking you to help us understand if it is possible to use mobile phones as a way to get more infants vaccinated. We will ask questions about SMS messages and M-PESA. If you agree to take part we will have a discussion that will last up to 2 hours. During this discussion, we will have one person asking questions to lead the discussion in the local language [*give name*]. One person will take notes notes [*give name*]. We will also be

using a tape recorder to remind us of the details of the discussion later on. We will turn off the tape recorder at any time that you request us to do so.

At the end of the discussion we will record your age, years of education, number of previous pregnancies, and whether you own a mobile phone.

Potential Harm, Injuries, Discomforts or Inconvenience, Risks: The risks of this study are low. There is a small risk your opinions might not be kept private if someone from the group shares the discussion, but we will discuss the importance of confidentiality at the beginning of the session.

Potential Benefits

There is no direct benefit to you from joining this study. Your opinions will be used to help design a research study that uses mobile phones to increase the number of kids getting vaccines. *)*

Confidentiality

During the discussion we will take handwritten notes and also tape record the session. We will not record participants' names during note taking. Instead we will assign numbers to individuals that will be matched against the responses. The notes will be translated into English if needed, and entered into a computer. No names will be entered into the computer. Tapes will be translated and transcribed. The tapes will then be destroyed. Where we use quotes from the discussions they will be designated by number. No quotes will be traceable to a specific person. All study materials will be kept in a locked cabinet or password protected computer at the KEMRI/CDC center in Kisian. Your name and identity will not be shown in any reports about this study.

Reimbursement

We will give you Ksh 300 to help pay for your time and travel costs. We will also provide refreshments during the session.

Participation

You do not have to take part in this study. You can decide to stop being part of this study at any time after you start. You don't have to answer any questions you don't want to. Before deciding whether you want to take part, please feel free to ask any questions. The health care you receive at area clinics, including the vaccines your child gets, will not be affected by your decision to take part, or not take part, in this study today

If you have any further questions or concerns

If you have questions or complaints as a result of being in this study please contact Dr. Frank Odhiambo, head of the KEMRI/CDC Kisian DSS, off of Kisumu-Busia Highway, P.O.

Box 1578 40100 or call 057-2022929 EXT 413, 0711-444333. If you feel you have been harmed in any way, or if you have questions about your rights as a research subject, and want to talk about the study with someone who is not directly involved in this research project, please contact The Secretary, KEMRI Ethics Review Committee, P.O. Box 54840-00200, Nairobi; Tel: 020-2722541, 0722205901, 0733400003; Email address: erc@kemri.org

Do you have any questions for me? Do you want to take part in this research study?

Your signature (or mark) on this form means:

- I have been informed about the study's purpose, procedures, possible benefits, and risks.
- I have been given the chance to ask questions before I sign.
- I have agreed to be in this study of my own free choice.

Name of Parent/Guardian: _____

Signature of Parent/Guardian: _____ Date:_____
(Put "X" if cannot sign name)

Name of Person administering the consent: _____

Signature of person administering consent: _____ Date: _____

(For those who are not able to read, a witness, who is not a family member or study staff, must verify and sign below.)

I have read and explained the consent form to the person named above and watched them indicate consent with a mark.

Name of Interpreter/Witness: _____

Signature of Interpreter/Witness: _____Date _____

Give one copy to the participant and keep one copy in study record

Appendix 7. Informed consent for the randomized controlled trial

KEMRI/CDC AND JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

Study Title: Randomized Controlled Trial of the Impact of Mobile Phone Delivered Reminders and Travel Subsidies to Improve Childhood Immunization Coverage Rates and Timeliness in western Kenya

Investigators: Daniel Feikin, Principal Investigator, Johns Hopkins School of Public Health/International Vaccine Access Center; CDC/National Center of Emerging and Zoonotic Infectious Diseases; Frank Odhiambo, KEMRI/CDC; Benard Ochieng, KEMRI/CDC; Dustin Gibson, Johns Hopkins School of Public Health/International Vaccine Access Center; David Obor, KEMRI/CDC; Danet Opot, KEMRI/CDC; Kayla Laserson, Center for Disease Control and Prevention; Amanda Glassman, Center for Global Development; Andrew Zeitlin, Georgetown Public Policy Institute and Center for Global Development, Dagna Constenla, Johns Hopkins School of Public Health/International Vaccine Access Center; Orin Levine, Bill and Melinda Gates Foundation; Tabu Collins, Kenya Ministry of Public Health and Sanitation, Division of Vaccines and Immunizations.

Study Location: Siaya County and neighboring villages

PI Version Date: 11 February 2013

Flesch-Kincaid readability level: 7.2
English version

Introduction

My name is _____ and I am working with researchers from KEMRI/CDC and Johns Hopkins School of Public Health; USA. We are here to find out if you would like to be in a research study that tries to get more infants vaccinated. I am going to give you some information about what we are doing. If there is anything you don't understand please ask me to stop and I will take time to explain. There will be time at the end for you to ask questions. After answering your questions, I will ask you if you want to join the study.

Purpose of study

We are doing this study because many Kenyan infants get their vaccines late or not at all. We are studying if we can use mobile phones to encourage mothers to bring children on time for their first three vaccines. This study is important because vaccines can protect infants from getting sick and dying. We want to explore ways to get more children vaccinated.

Why you are being asked to take part

We are asking you to join this study because you have a child who was born in the last month, is due to get his/her regular vaccines at 6 weeks of age and you live in one of the study villages. We anticipate 2,800 mothers and infants to join this study from this area.

Study Procedures

- You will be randomized to one of four groups. Randomization means it will be selected by chance, like using a coin flip. You will have an equal chance of being in each of the four groups. Your village and community leaders were part of the assigning of villages to the four groups to make sure it was done fairly. You cannot change the group you are in because it is based on the village where you live now. This means all mothers and children from your village will be in the same group. Each group will have a different way of using mobile phones to encourage immunization. We want to compare the 4 groups to see which is the best way to get children their vaccines on time.

If you join this study, this is what will happen during the next 9 months:

- Today, you will provide your child's name and date of birth.
- Today, we will ask for your mobile phone number or that of someone who has a phone that you have easy access to.
- Today, you will get a SMS message congratulating you for joining our study.
- Today, you will get a list of places that offer child immunizations in the area where the study takes place.
- Within the next 3 weeks, someone from the study team will come to your home and ask you questions about vaccines, mobile phones, and mobile-money. We may also take your infant's height and weight. This visit should take about 30 minutes.
- When you bring your child to the clinic for the first 3 doses of vaccine, scheduled to be given at 6, 10 and 14 weeks of age, we will collect some information. You should bring your MCH booklet with you. This will take about 5 minutes each time.
- When your child is 6 months old, we will come to your house. We will ask questions about your child's vaccinations, health, your household, SMS messages, and how you liked this study. We will weigh and take the height of your child. We will look at your maternal and child health card. This should take about 30 minutes.
- When your infant is between 9-12 months old, we will then come to your house to ask questions about immunizations. We will look at your maternal and child health card. This should take about 10 minutes.
- If your household is part of the HDSS, we will link these data to the HDSS data.
- Your village is in **Group 4**. We will send you 2 SMS reminders before each of the first 3 scheduled vaccine visits. We will send the first SMS 3 days before the vaccine is due and the second SMS on the day before the vaccine is due. When you bring your infant for vaccine, we will write down that your infant was vaccinated. If you bring your infant within 2 weeks of the expected immunization date, you will be given 200 Ksh by the mobile-money network of your choice, within 24 hours. In order to get this, you must bring your infant to

one of the clinics on the list where the study is working. If you bring your child in for vaccines later than 2 weeks after the expected date, you will not get the 200 Ksh. We will help you sign up for an account for mobile-money if you do not have one already.

Potential Harms, Injuries, Discomforts, Inconveniences or Risks

The risks from being in this study are small. Some people might find the questions asked of them take too much time out of their day. Vaccine jabs might cause brief pain to your child, as usual. But no new or experimental vaccines will be given in this study – only the regular, safe vaccines usually given by the Ministry of Health. There is a small chance your personal information may be revealed to people not in the study. We will do our best to prevent this.

Potential Benefits

Possible benefits to your child include getting him/her vaccinated on time. Vaccines can prevent disease and death. We will refer you to nearest clinic if your child does not have all vaccines by 6 months of age, but will not provide transportation or pay for any healthcare costs. We will give the results of the study to Ministry of Health to help improve child vaccinations in Kenya. The results might also help other African children to get their vaccines on time.

Confidentiality

We will try to keep your personal information as private as possible. After you decide to take part, you will receive a study number. This number will be used to label all study materials, rather than using your name. All study materials will be kept in a locked cabinet or password protected computer at the KEMRI/CDC center in Kisian. Your name and identity will not be shown in any reports about this study. We will not share your name or mobile phone number to anyone else besides the KEMRI/CDC staff involved in this study.

Participation

You do not have to take part in this study. You can decide to stop being part of this study at any time after you start. You don't have to answer any questions you don't want to. The health care you receive at area clinics, including the vaccines your child gets, will not be affected by your decision to take part, or not take part, in this study today. Before deciding whether you want to take part, please feel free to ask any questions.

Who do I call if I have questions or complaints?

If you have questions or complaints as a result of being in this study please contact Dr. Frank Odhiambo, head of the KEMRI/CDC Kisian DSS, off of Kisumu-Busia Highway, P.O. Box 1578 40100 or call 057-2022929 EXT 413, 0711-444333. If you feel you have been

harmed in any way, or if you have questions about your rights as a research subject, and want to talk about the study with someone who is not directly involved in this research project, please contact The Secretary, KEMRI Ethics Review Committee, P.O. Box 54840-00200, Nairobi; Tel: 020-2722541, 0722205901, 0733400003; Email address: erc@kemri.org

Do you have any questions for me? Do you want to take part in this research study?

Your signature (or mark) on this form means:

- I have been informed about the study's purpose, procedures, possible benefits, and risks.
- I have been given the chance to ask questions before I sign.
- I have agreed to be in this study of my own free choice.

Name of child:_____ Date of birth: _____

Name of Parent/Guardian: _____

Signature of Parent/Guardian: _____ Date:_____

(Put "X" if cannot sign name)

Name of Village Reporter/Person administering the consent: _____ _____

Signature of person administering consent: _____ Date: _____

(For those who are not able to read, a witness, who is not a family member or study staff, must verify and sign below.)

I have read and explained the consent form to the person named above and watched them indicate consent with a mark.

Name of Interpreter/Witness: _____

Signature of Interpreter/Witness: _____Date _____

Give one copy to the participant and keep one copy in study records

Appendix 8. Bivariate and multivariate analyses for predictors of severely underimmunized infants as compared to infants receiving all vaccinations on time[1]

Characteristic	Crude RR (CI)	p value	Adj RR (CI)	p value
Mother's age (years)				
15-24	Ref.		Ref.	
25-29	1.46 (1.08-1.98)	0.015	1.40 (1.04-1.89)	0.029
≥30	2.64 (2.05-3.41)	<0.001	2.17 (1.67-2.84)	<0.001
Mother's education (years)				
0-8	Ref.		Ref.	
9-12	0.53 (0.41-0.68)	<0.001	0.69 (0.53-0.90)	0.006
13+	0.21 (0.08-0.55)	0.001	0.30 (0.12-0.79)	0.015
Mother's English reading ability				
Not at all	Ref.		Ref.	
With Difficulty	0.66 (0.50-0.86)	0.002	0.96 (0.75-1.22)	0730
Easily	0.37 (0.28-0.50)	<0.001	0.78 (0.57-1.05)	0.105
Marital status				
Single/Divorced/Widowed	Ref.		Ref.	
Monogamous Married/Cohabitating	1.46 (1.03-2.06)	0.034	1.23 (0.88-1.72)	0.217
Polygamous Married/ Cohabitating	1.82 (1.17-2.82)	0.007	1.35 (0.91-2.00)	0.131
Children < 5 years old in house				
≤ 1	Ref.		Ref.	
2	1.50 (1.17-1.92)	0.001	1.17 (0.92-1.50)	0.205
≥3	1.43 (1.01-2.01)	0.044	1.02 (0.72-1.42)	0.930
Household size (no. of people)				
≤4	Ref.		Ref.	
>4	1.62 (1.29-2.02)	<0.001	1.20 (0.94-1.52)	0.136
Socioeconomic status[2]				
Bottom 40%	Ref.			
Upper 60%	0.81 (0.65-1.01)	0.060		
Mother's mobile phone ownership				
Owns Phone	Ref.		Ref.	
Has Access/None	0.56 (0.44-0.70)	<0.001	0.69 (0.55-0.86)	0.001
Distance to clinic (km)				
≤ 2	Ref.			
>2	1.25 (0.99-1.56)	0.351		
Child's age (months)				
12-18	Ref.			
>18 - 24	1.10 (0.88-1.37)	0.390		
Child's gender				
Female	Ref.			
Male	0.96 (0.77-1.20)	0.730		

Abbreviation: RR, risk ratio

[1] Severely underimmunized infants had greater than 90 days underimmunized and were delayed for three of five vaccines (BCG, pentavalent1, pentavalent2, pentavalent3, measles). Comparison group is infants receiving all vaccines on time (n=655)

[2] Socioeconomic status derived from Principal Components Analysis of household possessions

Appendix 9. Simple and multiple linear regressions for days vaccine delayed

	Pentavalent1[1]		Pentavalent3 [1]		Measles[1]	
	SLR	MLR	SLR	MLR	SLR	MLR
Mother's age (years)	β (SE)	β (SE)	β (SE)	β (SE)	β (SE)	β (SE)
15-24	*Ref.*		*Ref.*	*Ref.*	*Ref.*	
25-29	2.57 (1.45)		2.56 (2.41)	1.97 (2.48)	-0.03 (2.82)	
≥30	2.83 (1.47)		**11.8 (2.45)**	**9.95 (2.56)**	4.63 (2.91)	
Mother's education						
0-8 years	*Ref.*		*Ref.*		*Ref.*	
9-12 years	-1.50 (1.26)		**-8.01 (2.08)**		**-5.37 (2.44)**	
13+ years	-3.98 (2.77)		**-10.4 (4.46)**		**-16.6 (5.22)**	
Mother's English reading						
Not at all	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	**-4.26 (2.30)**	**-4.26 (2.30)**	**-9.52 (3.92)**	**-8.32 (4.14)**	**-10.2 (4.66)**	**-9.69 (4.86)**
Easily	**-5.70 (2.23)**	**-5.70 (2.23)**	**-15.8 (3.78)**	**-13.5 (4.04)**	**-15.2 (4.48)**	**-14.7 (4.69)**
Marital status						
Single/Divorced	*Ref.*		*Ref.*		*Ref.*	
Monogamous Married	0.34 (1.67)		1.61 (2.77)		-0.41 (3.20)	
Polygamous Married	0.01 (2.36)		6.71 (3.94)		4.23 (4.63)	
Children < 5 years old in house						
≤ 1	*Ref.*		*Ref.*	*Ref.*	*Ref.*	
2	1.75 (1.29)		**6.17 (2.16)**	**5.49 (2.21)**	2.25 (2.53)	
≥3	3.51 (1.88)		5.86 (3.14)	3.98 (3.23)	5.27 (3.70)	
Household size						
≤4 people	*Ref.*		*Ref.*		*Ref.*	
>4 people	**2.46 (1.20)**		**5.12 (2.01)**		4.26 (2.36)	
Socioeconomic status[2]						
Bottom 40%	*Ref.*		*Ref.*	*Ref.*	*Ref.*	
Top 60%	-1.86 (1.23)		**-5.20 (2.05)**	**-5.34 (2.09)**	-2.13 (2.40)	
Mother's mobile phone						
Has Access/None	*Ref.*		*Ref.*		*Ref.*	
Owns Phone	**-2.50 (1.20)**		**-4.13 (2.02)**		**-4.86 (2.36)**	
Distance to clinic (km)						
≤ 2	*Ref.*		*Ref.*	*Ref.*	***Ref.***	***Ref.***
>2	1.02 (1.25)		**5.78 (2.08)**	**4.74 (2.08)**	**5.86 (2.42)**	**5.49 (2.42)**
Child's age (months)						
12-18	*Ref.*		*Ref.*	*Ref.*	*Ref.*	*Ref.*
>18 - 24	1.12 (1.20)		**6.44 (2.00)**	**6.33 (2.05)**	**13.48 (2.33)**	**13.79 (2.40)**
Child's gender						
Female	*Ref.*		*Ref.*		*Ref.*	
Male	-1.04 (1.20)		-0.23 (2.01)		-1.09 (2.35)	

Abbreviations: MLR, multiple linear regression; SLR, simple linear regression; yrs, years

[1] Days delayed are continuous. Infants timely vaccinated have 0 days delay. Excludes infants who did not receive vaccination. Bolded beta coefficients and confidence intervals indicate $p<0.05$

[2] Socioeconomic status derived from Principal Components Analysis of household possessions

Appendix 10. Mobile Solutions for Immunization (M-SIMU) enrollment and screening form

1.1Village #(from study ID)_____ 1.2 Compound#(from study ID)____
1.3 Compound Name: [__][__] [__][__] [__][__][__][__][__][__][__][__][__][__] [__][__] [__][__][__][__][__][__][__]
1.4 Study ID: [__][__][__]---[__][__][__][__]---[__][__]
1.5 Child First Name: [__][__] [__][__] [__][__][__][__][__][__][__][__][__][__]
1.6 Child Juok Name: [__][__] [__][__] [__][__][__][__][__][__][__][__][__][__]
1.7 Child Last Name: [__][__] [__][__] [__][__][__][__][__][__][__][__][__][__]
1.8 Is Child's HH currently living in within DSS borders? YES….NO…
1.8.1 IF YES, Child's Location ID (FOR HH CURRENTLY LIVING IN): [__][__][__]---[__][__][__][__]---[__][__]---[__]
1.8.2 IF NO, provide village name and describe where located
1.9 GPS Coordinates:_____
1.10 Child's DOB according to Mother/caretaker [__][__] / [__][__] / [__][__][__][__]
1.11 Is enrolled mother/caregiver still alive? ALIVE AND PRESENT……MOVED AWAY…….DEAD…..DK
1.11.1 If ALIVE to 1.11, Mother First Name: [__][__][__][__][__][__][__][__][__][__]
1.11.1.a Mother Last Name: [__][__] [__][__] [__][__][__][__][__][__][__][__]
1.11.1.b Phone number used in MSIMU [__][__][__][__][__][__][__][__][__][__]
1.11.2 If MOVED AWAY OR DEAD to 1.11, what is relationship of new primary caregiver
to infant (Circle one)…. MOTHER….FATHER…. GRANDMOTHER…
…….STEPMOTHER…….AUNT…...NA…OTHER (SPECIFY) _____
1.11.3 If DK to 1.11, elaborate on why DK was picked (open-ended)_____
1.12 Is enrolled child (Circle One): ALIVE…..DEAD…..UNKNOWN
1.12.1 If DIED, date of death? [__][__] / [__][__] / [__][__][__][__]
1.12.2 If ALIVE OR UNKNOWN, Did infant move from compound in the study ID?
YES……NO……CANT FIND CHILD
1.12.2.b If YES to 1.12.2, what village?(open-ended)_____

Immunization history - *ask care-taker*

2.1. **ende nyathini ne oyudo chanjo mar geng'o tuoche, e klinik ata kane sirikal okelo chanjo mar nyithindo e gweng?**
(Did (name) ever receive any vaccination to prevent him/her getting diseases, including vaccination received in a national immunisation day campaign?) ----○ Ee (Yes) ○ Ooyo (No) ○ *Akia (Don't know)

*If **"YES" or "Don't Know"**, then Skip to Question #2.3. If "**NO**" go to Q2.2

2.2. **a ooyo to ere gimomiya pod ok oter nyathi chanjo? (**If No, what's the reason?**)**

○ nengo ne malo (cost was high) ○ kar chanjo bor (vaccination site far) ○ Din ok oyie (against faith/religion)
○ aluoro (fear of vaccination) ○ chanjo ok tii (don't work for me) ○ NA
○ ler machielo (other, specify)

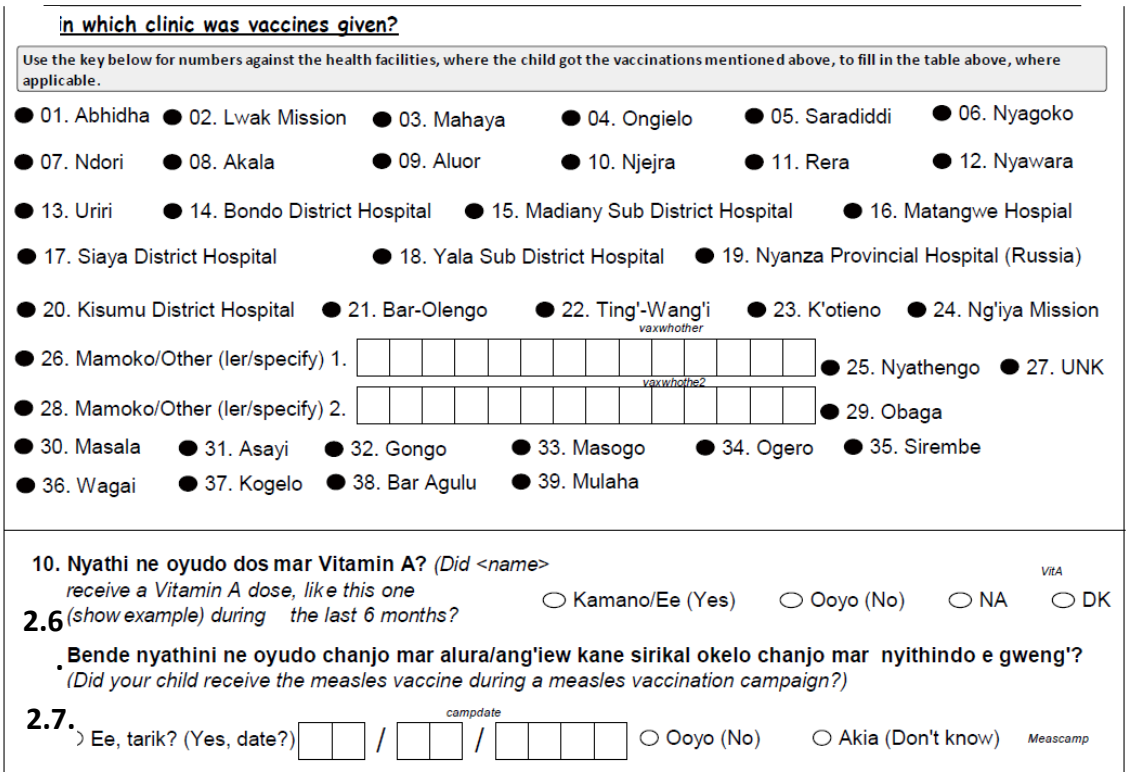
2.3. **e in gi kadi mar Klinik ma ondikie chanjo mosechiw?**
(Do you have a card where (name's) vaccinations are recorded down? **Ka iyei, nyisa go?** (if YES, may I see it please?) ○ Ee (Yes, seen) ○ Eee, ok aneno(Yes, not seen) ○ Ooyo, onge kad (No card)

If card is NOT available mark **NA** for questions **4 - 5** and proceed to the verbal report questions;
If AVAILABLE, observe and read from the card the following immunizations questions.

2.4 Where card is available, fill the "FROM CARD" column Only using the information from the card, in the table below. If a card is not available or does not have a specific vaccination, obtain from the verbal report and mark "verbal report" column. Fill HF using codes

	FROM CARD		VERBAL		
Vaccine	Given: Yes/No	Date Received	Given:Yes/No/DK	Age at vaccination	Health Facility where given
BCG				weeks	
Polio-Birth				weeks	
Polio1				weeks	
Polio2				weeks	
Polio3				weeks	
Penta1				weeks	
Penta2				weeks	
Penta3				weeks	
PCV1				weeks	
PCV2				weeks	
PCV3				weeks	
Measles					

2.5 If measles vaccine given late (age received >10 months)), what are reasons for delay?.....COST WAS HIGH…..CLINIC TOO FAR…….DIDN'T KNOW VAC DATE….FORGOT ABOUT VACCINATION….TRAVELLING…….. …..VACCINES NOT IMPORTANT VACCINE NOT IN STOCK …..OTHER (SPECIFY)_____



2.8 What factor was most important in determining which clinic you brought your infant to for immunizations?...

….COST….DISTANCE….STAFF TREAT ME WELL… VACCINES ALWAYS IN STOCK…..NEW CAREGIVER, DID NOT BRING……OTHER (SPECIFY)_____

2.9 How far is the nearest Mpesa/mobile money agent from your compound in walking time?.....<10 minutes……10-21 minutes…..20-40 minutes….41-60 minutes….> 1 hour….DK

2.11 Are you registered with MPESA/ORANGE/YU/or other mobile money network?....YES…NO….DK

If YES to 2.11, when did you register for the mobile money network? <1 MONTH AGO…..1-3 MONTHS AGO….3-6 MONTHS AGO….6-12 MONTHS AGO…> 1 YEAR AGO

2.12 (Aside from SMS and small money…*Only say this for those in intervention arms*), what motivated you to bring your child in for immunization?.....FAMILY TOLD ME….VACCINE GOOD FOR KID….OTHER MOTHERS DO IT….CHW TOLD ME…..CLINIC STAFF TOLD ME… ….OTHER_____

For those in arm 1 (control), skip to question 7.1

FOR THOSE IN ARMS 2-4 (SMS, 75ksh, 200ksh)

5.1 Did you receive SMS reminders for ANY OF your child's immunization appointments?

...YES…NO….NEW PRIMARY CAREGIVER…DON'T REMEMBER

5.1.1 If NO to 5.1, why do you think you did not receive REMINDERS? NEW PRIMARY CAREGIVER…..PERSON WHO OWNED PHONE DID NOT GIVE…..KEMRI DID NOT SEND…I MOVED AWAY….PERSON WHO OWNED PHONE MOVED AWAY …OTHER (SPECIFY)_____THEN *SKIP TO Q6.1*

5.1.2 IF DON'T REMEMBER OR NEW PRIMARY CAREGIVER for 5.1, **SKIP TO Q6.1**

5.2 For MEASLES vaccine, whose mobile phone were reminders sent to? MINE….SOMEBODY ELSE

5.2.1 If MINE for 5.2, how many SMS reminders did you receive for Measles vaccine …0…1……2…..3…. DK

5.2.1.a If <2 SMS for Measles, Why do you think you did not receive some of the SMS messages?.... I WAS AWAY….PHONE NOT CHARGED….LOST/BROKE PHONE…KEMRI DID NOT SEND…VACCINATED AFTER RECEIVING FIRST REMINDER…VACCINATED INFANT BEFORE ANY REMINDER received…OTHER (SPECIFY)____

5.2.2 If SOMEBODY ELSE for 5.2, how many SMS reminders did you receive for Measles vaccine? ...0..1..2..3..DK

5.2.2.a If <2 SMS for Measles, Why do you think you did not receive some of the SMS messages?.... OWNER OF PHONE AWAY….OWNER OF PHONE FORGOT TO TELL ME…..I WAS AWAY….PHONE NOT CHARGED….LOST PHONE…KEMRI DID NOT SEND……OTHER (SPECIFY)____

5.3 Overall, did the SMS reminders influence your decision to bring your child for immunization? YES….NO….DK

5.4 Overall, what did you think of the number of SMS sent to you? TOO MANY…..TOO LITTLE….JUST RIGHT….MOBILE PHONE SHARED…..DK

5.5 How did you find the length of the SMS reminders….TOO SHORT, RIGHT LENGTH, TOO LONG…MOBILE PHONE SHARED….DK

5.6 What was your opinion of the small phrase at the end of the reminder? ENJOYED IT….DIDNT LIKE IT…DON'T REMEMBER IT…MOBILE PHONE SHARED….NO OPINION

FOR THOSE IN ARMS 3 and 4 (75ksh and 200ksh)

6.2 Did you receive any payments through mobile money as part of this study....YES….NO…DON'T REMEMBER…NEW PRIMARY CARE GIVER

6.2.1 If NO, why do you think you did not receive payment? NEW PRIMARY CAREGIVER…..PERSON WHO OWNED PHONE DID NOT GIVE…..KEMRI DID NOT SEND…I MOVED AWAY….PERSON WHO OWNED PHONE MOVED AWAY…… DID NOT VACCINATE INFANT…..INFANT VACCINATED LATE …OTHER (SPECIFY)_____ ***then SKIP to Q7.1***

6.2.2 IF DON'T REMEMBER OR NEW PRIMARY CAREGIVER for 6.2, **SKIP TO Q7.1**

6.3 For Measles vaccine, whose mobile phone was money sent to? MINE….SOMEBODY ELSE

6.3.1 If MINE for Q6.3, Did you receive the payment for measles vaccine?: YES…NO…DON'T REMEMBER….

6.3.1.a If YES for 6.3.1, when did you cash out the incentive? SAME DAY…..1-3 DAYS….>3 DAYS…..NOT CASHED OUT

6.3.1.a If NO for 6.3.1, why do you think you didn't receive a payment…. ….PHONE WAS LOST/BROKE….KEMRI DID NOT SEND….MY CHILD WAS VACCINATED LATE… DIDN'T RECEIVE MEASLES VACCINE YET….DK….OTHER(SPECIFY)_____

6.3.2 If SOMEBODY ELSE for Q6.3, Did you receive the payment for measles vaccine?: YES…NO…..DON'T REMEMBER

6.3.1.a If YES for 6.3.2, when did you cash out the incentive? SAME DAY…..1-3 DAYS….>3 DAYS…..NOT CASHED OUT

6.3.1.a If NO for 6.3.1, why do you think you didn't receive a payment….OWNER OF PHONE AWAY…OWNER OF PHONE WITHHELD MONEY ….PHONE WAS LOST….KEMRI DID NOT SEND….MY CHILD WAS VACCINATED LATE….DK….OTHER (SPECIFY)

6.4 Did our telling you that you would receive small money influence your decision to bring your child for immunizations?..... YES…NO… ….DK……NOT PRIMARY CAREGIVER ….DIDNT KNOW WOULD RECEIVE PAYMENT

6.5 What did you use the MPESA for?" with Answers TRANSPORT COST…FOOD…AIRTIME…HOUSING EXPENSES…SCHOOL EXPENSES….MEDICINE…NOT USED BY MOTHER…..OTHER….DK (Select all that apply)

6.6 How was your experience in receiving cash through Mpesa/ZAP/Orange/Yu-Cash and KEMRI/CDC?..... VERY

POSITIVE….SOMEWHAT POSITIVE…..NEUTRAL….SOMEWHAT NEGATIVE….VERY NEGATIVE

6.9 For future vaccines for this child or other children, would you be more/less/same likely to bring them in for vaccination if you do not get any small money?..... MORE LIKELY…….LESS LIKELY……THE SAME……DK

6.10 Would you have preferred to receive airtime over mobile-money cash (Same KSH for both)?....YES….NO…DK….

6.11 Between SMS reminders and incentives, what influenced you most in bringing your child for vaccination" ….SMS REMINDER….INCENTIVE….INCENTIVE AND REMINDER EQUALLY….NEITHER

****FOR ALL STUDY PARTICIPANTS

7.1 Does your child usually sleep under an INSECTICIDE treated bednet?.....YES…..NO……DK

7.1.1 *If YES for 7.1,* Did your child sleep under an INSECTICIDE treated bed net last night? ..... YES…..NO…..DK

7.1.2 *If NO to 7.1*, Does your child usually sleep under a bed net? ..... YES…..NO…..DK

7.1.2.b *If YES for 7.1.2,* Did your child sleep under an bed net last night? ..... YES…..NO…..DK

7.2 How many times has your infant been to the health facility for an illness (e.g. fever, respiratory problem, diarrhea) in the last 2 weeks (excluding immunization visits)? [__][__]

7.3 How many times has your infant been hospitalized in the last 1 month (e.g. fever, respiratory problem, diarrhea) (excluding immunization visits)?...[__] [__]

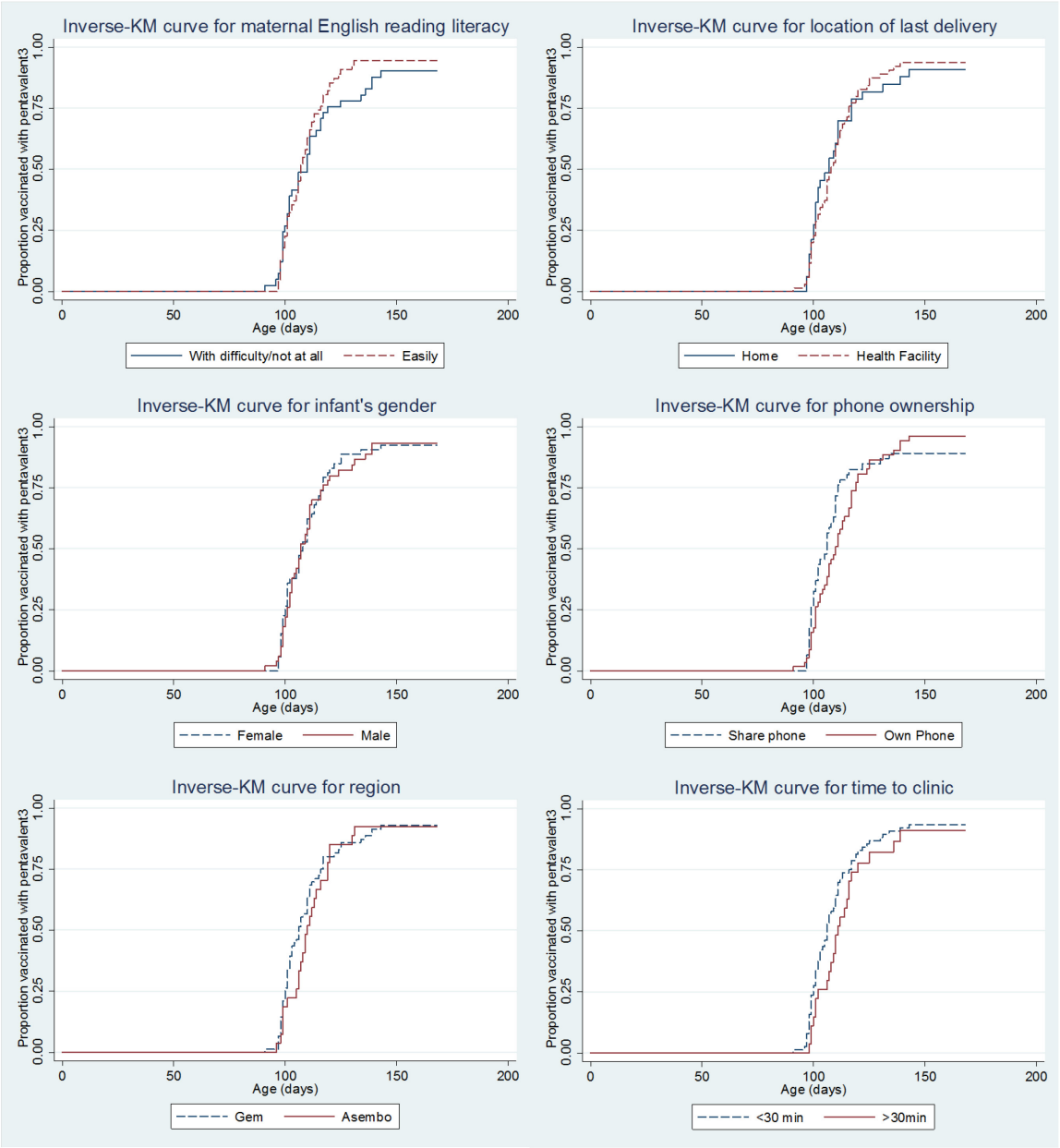
7.4 FOR CI: Are you able to take child's height? (CIRCLE ONE)….YES…..NO

If YES, Child's Height (cm) [__] [___] [___] **.** [__]

If NO, what was reason?....CHILD SLEEPING….MOTHER REFUSED….OTHER(SPECIFY)_____

Comments_____

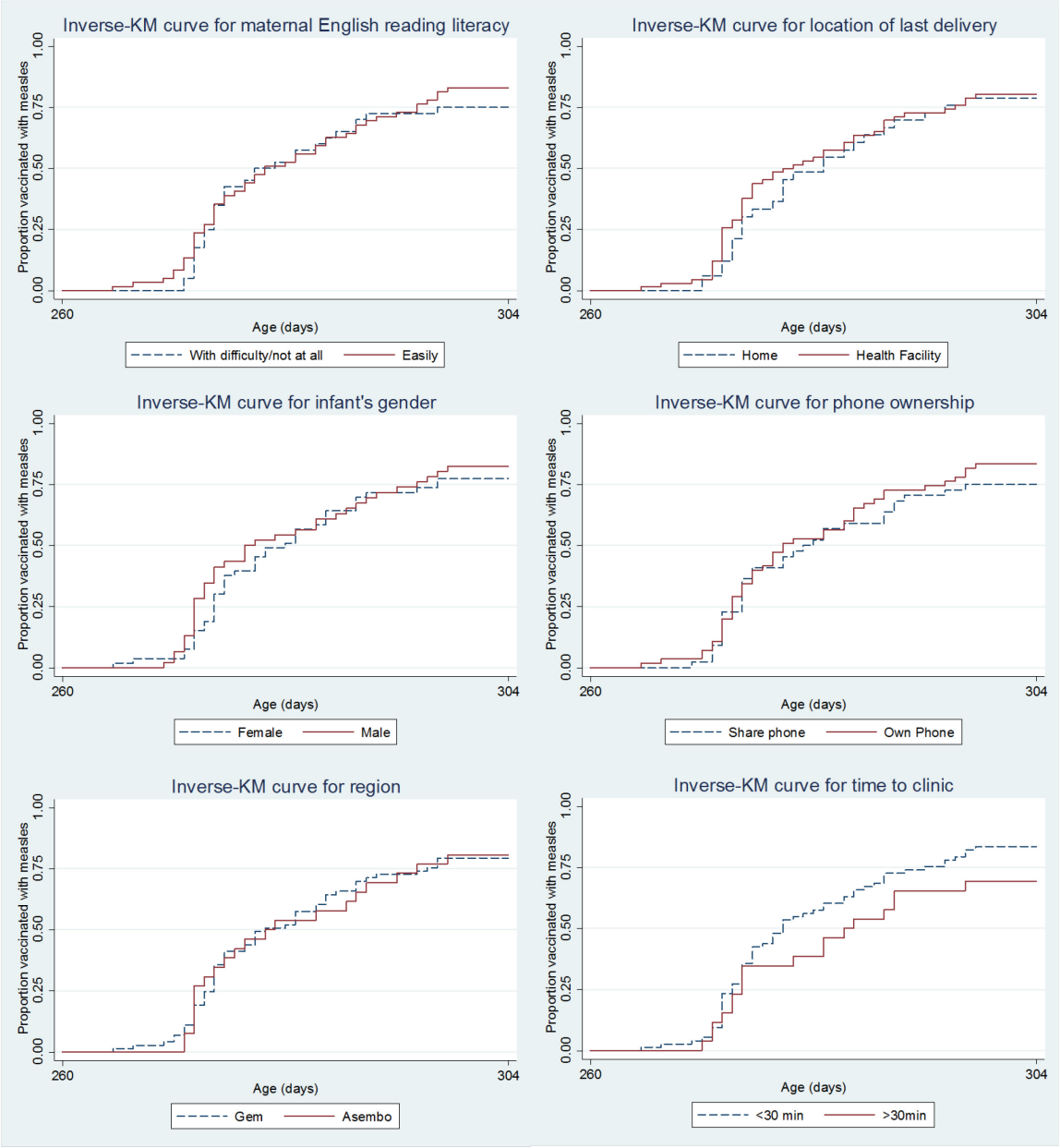
Appendix 11. Inverse Kaplan-Meier curves for time to pentavalent3 by selected demographic variables using intention-to-treat delivery of short message system (SMS) reminders



Abbreviation: KM, Kaplan-Meier

CAPTION: No curves were statistically significant using overall test of equality

Appendix 12. Inverse Kaplan-Meier curves for time to measles by selected demographic variables using intention-to-treat delivery of short message system (SMS) reminders



Abbreviation: KM, Kaplan-Meier

CAPTION: No curves were statistically significant using overall test of equality

Appendix 13. Unadjusted and adjusted risk ratios for vaccination within two weeks of schedule

		Study Arm			
		Control	SMS	SMS + 75 KSH[1]	SMS + 200KSH[1]
Pentavalent1	No. of participants[2]	22	31	27	24
	No.Vaccinated[2]	21	27	26	23
	% (95% CI)	95.5 (77.2-99.9)	87.1 (70.2-96.4)	96.3 (81.0-99.9)	96.0 (79.7-99.9)
	Unadjusted				
	RR (95% CI)	1 (Reference)	0.91 (0.77-1.08)	1.01 (0.91-1.12)	1.01 (0.90-1.12)
	P value		0.281	0.868	0.920
	Adjusted[3]				
	RR (95% CI)	1 (Reference)	0.95 (0.85-1.05)	1.02 (0.91-1.12)	1.03 (0.92-1.16)
	P value		0.321	0.641	0.580
Pentavalent2	No. of participants[2]	22	30	27	24
	No. Vaccinated[2]	20	26	24	24
	% (95% CI)	90.9 (70.8-98.9)	86.7 (69.3-96.2)	88.9 (70.8-97.6)	100 (85.7-100.0)[4]
	Unadjusted				
	RR (95% CI)	1 (Reference)	0.95 (0.75-1.21)	0.98 (0.82-1.16)	1.10 (0.97-1.25)
	P value		0.694	0.801	0.146
	Adjusted[3]				
	RR (95% CI)	1 (Reference)	0.91 (0.69-1.21)	0.95 (0.76-1.19)	1.07 (0.87-1.30)
	P value		0.536	0.661	0.518
Pentavalent3	No. of participants[2]	22	30	27	24
	No. Vaccinated[2]	15	21	22	24
	% (95% CI)	68.2 (45.1-86.1)	70.0 (50.6-85.3)	81.5 (61.9-93.7)	100 (85.7-100.0)[4]
	Unadjusted				
	RR (95% CI)	1 (Reference)	1.03 (0.68-1.56)	1.20 (0.80-1.77)	1.46 (1.01-2.12)
	P value		0.902	0.379	0.043
	Adjusted[3]				
	RR (95% CI)	1 (Reference)	1.04 (0.67-1.63)	1.21 (0.78-1.88)	1.49 (0.99-2.25)
	P value		0.854	0.397	0.059
Measles	No. of participants[2]	22	28	25	24
	No. Vaccinated[2]	13	17	13	20
	% (95% CI)	59.1 (36.4-79.3)	60.7 (40.6-78.5)	52.0 (31.3-72.2)	83.3 (62.6-95.3)
	Unadjusted				
	RR (95% CI)	1 (Reference)	1.03 (0.62-1.71)	0.88 (0.52-1.50)	1.41 (0.91-2.19)
	P value		0.917	0.637	0.128
	Adjusted[3]				
	RR (95% CI)	1 (Reference)	1.11 (0.67-1.86)	0.89 (0.52-1.53)	1.50 (0.93-2.41)
	P value		0.677	0.675	0.099

Abbreviations: RR, risk ratio; SMS, short message system; KSH, Kenyan Schilling

[1] 85 KSH= 1 United States Dollar as of October 2014

[2] Participants must have been alive and not out migrated by the scheduled date of vaccination plus 2 weeks

[3] Adjusted for phone ownership, time to clinic, and region *a priori*

[4] One sided, 97.5% confidence interval

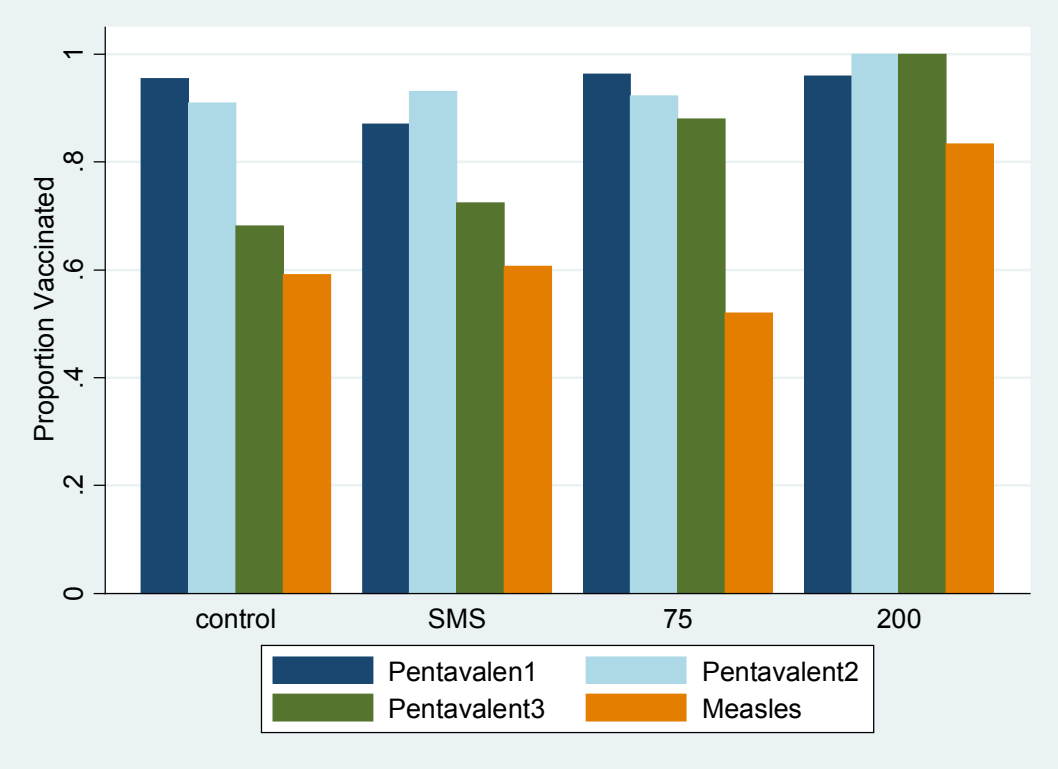
Appendix 14. Unadjusted and adjusted risk ratios for vaccination coverage

		Study Arm			
		Control	SMS	SMS + 75 KSH[1]	SMS + 200KSH[1]
Pentavalent3	No. of participants[2]	22	29	27	24
	Vaccinated[2]				
	No.	21	26	24	24
	% (95% CI)	95.5 (77.2-99.9)	89.7 (72.6-97.8)	88.9 (70.8-97.6)	100 (85.8-100.0)[5]
	Unadjusted				
	RR (95% CI)	1 (Reference)	0.94 (0.83-1.06)	0.93 (0.80-1.07)	1.05 (0.96-1.14)
	P value		0.322	0.341	0.288
	Adjusted[3]				
	RR (95% CI)	1 (Reference)	0.93 (0.81-1.08)	0.96 (0.80-1.14)	1.07 (0.94-1.22)
	P value		0.347	0.612	0.319
Measles	No. of participants[3]	22	28	25	24
	Vaccinated[3]				
	No.	18	20	18	23
	% (95% CI)	81.8 (51.3-86.8)	71.4 (51.3-86.8)	72.0 (50.6-87.9)	95.8 (78.9-99.9)[4]
	Unadjusted				
	RR (95% CI)	1 (Reference)	0.87 (0.63-1.20)	0.88 (0.66-1.16)	1.17 (0.96-1.43)
	P value		0.404	0.375	0.125
	Adjusted[4]				
	RR (95% CI)	1 (Reference)	0.94 (0.69-1.30)	0.92 (0.67-1.26)	1.26 (0.98-1.61)
	P value		0.728	0.614	0.067

Abbreviations: RR, risk ratio; SMS, short message system; KSH, Kenyan Schilling

[1] 85 KSH= 1 United States Dollar as of October 2014
[2] Participants must have been alive and not out migrated by 24 weeks
[3] Participants must have been alive and not out migrated by 10 months (303 days)
[4] Adjusted for phone ownership, time to clinic, and region *a priori*
[5] One sided, 97.5% confidence interval

Appendix 15. Immunization coverage within two weeks of scheduled date by study arm



CAPTION: Immunization coverage within two weeks of vaccination appointment date calculated for pentavalent1, pentavalent2, pentavalent3, and measles vaccines. Appointment date for pentavalent1 was 42 days of age. For pentavalent2, appointment date was calculated by adding 28 days (4 weeks) to date of pentavalent1 receipt. For pentavalent3, appointment date was calculated by adding 28 days to date of pentavalent2 receipt

DUSTIN GARRETT GIBSON

2240 E. Baltimore St
Baltimore, MD 21231
dgibso28@jhsu.edu
(919) 943-1095

CURRICULUM VITAE

EDUCATION

Aug. 2010 Present Doctoral Student in Global Disease Control and Epidemiology program
Johns Hopkins University- Bloomberg School of Public Health
Vaccine Science and Policy Certificate May 2012
Dissertation to be proposed: *The readiness, need for, and effect of mHealth interventions to improve immunization timeliness and coverage in rural western Kenya*
Advisor: Dan Salmon, PhD
Dissertation Readers: Alain Labrique, PhD; Harold Lehmann, MD; William Moss, MD

Jan. 2008- Aug. 2009 Certificate in Field Epidemiology
University of North Carolina at Chapel Hill

Aug. 2004- May 2006 M.S. Neuroscience
University of Michigan at Ann Arbor
Advisor: Denise Figlewicz, PhD

Sept. 2000- May 2004 B.S., Psychobiology Magna Cum Laude
B.A., Philosophy Magna Cum Laude
State University of New York at Binghamton
All University Honors
Honor's Thesis: *Postnatal Ethanol Exposure Reduces the Number of Parvalbumin Expressing Purkinje Cells in the Rat Cerebellum*
Advisor: Anna Klintsova, PhD

RESEARCH EXPERIENCE

Jan. 2011- Present Co-Principal Investigator
Johns Hopkins University-International Vaccine Access Center (IVAC)
KEMRI/CDC Research and Public Health Collaboration
Principal Investigator*:* Daniel Feikin, MD
The Mobile Solutions for Immunization (M-SIMU) study is a 152 village randomized controlled trial that aims to improve routine pediatric vaccine coverage and timeliness through use of reminders and subsidies delivered via a mobile phone system in rural western Kenya. Responsibilities include: formulate study design; synthesize study protocol, implement study, train and mentor junior staff; data analysis; serve as liaison with international collaborators

Apr. 2014-Present Co-Investigator
Johns Hopkins University-International Vaccine Access Center (IVAC)
KEMRI/CDC Research and Public Health Collaboration
Principal Investigators*:* Kate O'Brien, MD; Kyla Hayford, PhD
The Estimating Effective Vaccination Coverage with Immune Markers study is nested within the M-SIMU trial. The study's objective is to develop an accurate and field-friendly method to assess effective vaccination coverage in young children for tetanus and measles antibodies using dried blood spots and oral fluid as compared to venous serum. Responsibilities include contributions to study design, participant selection, and on-sight supervision

Oct. 2010-Sept. 2012 Research Assistant
Johns Hopkins University-International Vaccine Access Center (IVAC)
Principal Investigator*:* Daniel Feikin, MD
Conducted a systematic review/meta-analysis on the role that residential distance from health care facilities plays on vaccination coverage, antenatal and postnatal care attendance, delivery at a medical facility, and health seeking for acute and chronic conditions. Developed search criteria and conducted literature review using five databases; created inclusion/exclusion criteria for initial abstract review; trained two JHSPH students to assist with abstract review; managed large database; performed meta-analyses

June 2011-Present Research Assistant
Johns Hopkins University-International Vaccine Access Center (IVAC)
Principal Investigators*:* Laura Hammitt, MD; Maria Knoll, PhD
Performed statistical analyses for pilot study concerning pneumonia etiology in Kilifi, Kenya. Created tables and figures for peer-reviewed publication. This pilot study serves as basis for a 7-country case-control analysis study called Pneumonia Etiology Research for Child Health (PERCH). Member of the PERCH data analysis team.

July 2011-August 2011 Summer Research Assistant
Medical Research Council (MRC) at Basse, The Gambia
Principal Investigators: Grant Mackenzie, MD; Orin Levine, PhD
The MRC in Basse is a collection of laboratories and clinics with a staff of approximately 175 employees. They are responsible for demographic and disease surveillance for a population of over 150,000 people in rural Gambia. Using STATA 9.0, I wrote code to merge and clean databases and conduct descriptive statistical analyses for health care utilization patterns, pneumonia severity scores, and vaccination coverage. I also conducted analyses for a novel, and alternative, scoring paradigm for x-ray confirmed pneumonia. The results of this will be published in a peer reviewed journal.

Sept. 2006-
August 2010 Research Specialist
University of North Carolina at Chapel Hill
Principal Investigator*:* Luda Diatchenko MD, PhD
Lead molecular analyst for case-control study looking at genetic, molecular, physiological, and psychosocial determinants in women with Temporomandibular Joint Disorder; collect, analyze, and present molecular experiments; consent research participants; conduct clinical sensory testing

Jan. 2005-
May 2006 Graduate Student Research Assistant
Neuroscience Program at University of Michigan at Ann Arbor
Advisor*:* Denise Figlewicz, PhD
Studied the role of neurodegeneration in a murine model of Amyotrophic Lateral Sclerosis (ALS); performed data collection, analysis, and presentation; assisted with grant writing and paper submissions; efficient in statistics programs Prism3; routinely presented results in weekly lab meetings.

Jan. 2003-
May 2004 Undergraduate Research Assistant
Psychobiology Program at State University of New York at Binghamton
Advisor*:* Anna Klintsova*,* PhD
Explored role of alcohol intake on the developing nervous system of rat pups; completed senior year honor's thesis on the effect of postnatal alcohol exposure and its effect on Parvalbumin expressing Purkinje cells of the rat cerebellum; performed data collection and analysis; trained new lab personnel.

PEER- REVIEWED JOURNAL ARTICLES

1. Gibson, DG, Omondi B, Kagucia E, Odhiambo F, Levine O, O'Brien K, & Feikin D. Predictors of immunization coverage and timeliness in rural western Kenya. 2014. *Under preparation*

2. Gibson DG, Omondi B, Kagucia E, Odhiambo F, Winch P, Glassman A, Levine O, O'Brien K, & Feikin D. mHealth interventions to improve immunization: formative research findings and epidemiology of mobile phone ownership and SMS behavior in rural western Kenyan mothers. 2014. *Under review at Bull WHO.*

3. Gibson DG, Omondi B, Kagucia E, Odhiambo F, Winch P, Glassman A, Levine O, O'Brien K, & Feikin D. The Mobile Solutions for Immunization (M-SIMU) Trial: A Protocol for a cluster randomized controlled trial of the impact of mobile phone delivered reminders and travel subsidies to improve childhood immunization coverage rates and timeliness in western Kenya. 2014. *Manuscript under preparation*

4. Gibson, DG & Feikin, D. The distance decay effect on healthcare utilization: A systematic review and meta-analysis. 2014. *Manuscript under preparation*

5. Wakadha, H., Chandir, S., Were, E., Rubin, A., Obor, D., Levine, O., **Gibson, DG.**, Odhiambo, F., Laserson, K., Feikin D. The feasibility of using mobile-phone based SMS reminders and conditional cash transfers to improve timely immunization in rural Kenya. *Vaccine.* 2013 Jan 30;31(6):987-93. PMID: 23246258

6. Hammitt L, Kazungu S, Morpeth SC, Mwarumba S, Bett, A, **Gibson DG,** Brent A, Akech DO, Murdoch DR, Nokes DJ, Scott AG. A preliminary study of pneumonia etiology among hospitalized children in Kenya. *CID* PERCH supplemental issue. 2012 Apr;54 Suppl 2:S190-9. PMID: 22403235.

7. Slade GD, Smith SB, Zaykin DV, Tchivileva IE, **Gibson DG**, Yuryev A, Mazo I, Bair E, Fillingim R, Ohrbach R, Greenspan J, Maixner W, Diatchenko L. Facial pain with localized and widespread manifestations: separate pathways of vulnerability. *Pain*. 2013 Nov;154(11):2335-43. PMID: 23867732

8. Neely GG, Rao S, Costigan M, Mair N, Racz I, Milinkeviciute G, Meixner A, Nayanala S, Griffin RS, Belfer I, Dai F, Smith S, Diatchenko L, Marengo S, Haubner BJ, Novatchkova M, **Gibson D**, Maixner W, Pospisilik JA, Hirsch E, Whishaw IQ, Zimmer A, Gupta V, Sasaki J, Kanaho Y, Sasaki T, Kress M, Woolf CJ, Penninger JM. Construction of a global pain systems network highlights phospholipid signaling as a regulator of heat nociception. *PLoS Genet* 2012 Dec;8(12). PMID:23236288

9. Smith SB, Maixner DW, Greenspan JD, Dubner R, Fillingim RB, Ohrbach R, Knott C, Slade GD, Bair E, **Gibson DG**, Zaykin DV, Weir BS, Maixner W, Diatchenko L. Potential genetic risk factors for chronic TMD: genetic associations from the OPPERA case control study. *J Pain*. 2011 Nov;12(11 Suppl):T92-101. PMID: 22074755

10. Serohijos AW, Yin S, Ding F, Gauthier J, **Gibson DG**, Maixner W, Dokholyan NV, Diatchenko L. Structural basis for μ-opioid receptor binding and activation. *Structure*. 2011 Nov 9;19(11):1683-90. PMID:22078567

11. Neely G, Hess A, Costigan M, Keene A, Goulas S, Langeslag M, Griffin R, Belfer I, Feng Dai, Smith S, Diatchenko L, Gupta V, Xia C, Amann S, Kreitz S, Heindl-Erdmann C, Ly C, Arora C, Sarangi R, Dan D, Novatchkova M, Rosenzweig M, **Gibson DG**, Truong D, Schramek D, Zoranovic T, Cronin S, Angjeli B, Brune K, Dietzl G, Maixner W, Meixner A; Thomas W, PospisilikA, Alenius M, Kress M, Subramaniam S, Garrity P, Bellen H, Woolf C, Penninger JM. A genome-wide Drosophila screen for heat nociception identifies α2δ3 as an evolutionary conserved pain gene. *Cell*. 2010 Nov 12;143(4):628-38. PMID: 21074052

12. Gris P, Gauthier J, Cheng P, **Gibson DG**, Gris D, Laur O, Pierson J, Wentworth S, Nackley AG, Maixner W, Diatchenko L. A novel alternatively spliced isoform of the mu-opioid receptor: functional antagonism. *Molecular Pain.* 2010, 6:33. PMID: 20525224

13. Reimann F, Cox JJ, Belfer I, Diatchenko L, McHale DP, Drenth JPH, Dai F, Wheeler J, Sanders F, Wood L, Wu TX, Jaro K, Nikolajsen L, Männikkö M, Max MB, Kiselycznyk C, Poddar M, Morsche RHM, Smith S, **Gibson D**, Maixner W, Gribble F, Woods CJ. Pain perception in common painful conditions is altered by a nucleotide polymorphism in *SCN9A. Proc. Natl. Acad. Sci./ USA.;* 2010 Mar 16;107(11):5148-53. PMID: 20212137.

14. Nackley, A.G., Shabalina, S.A., Lambert, J.E., Conrad, M.S., **Gibson, D.G.,** Spiridinov, A.E., Satterfield, S.K. & Diatchenko, L. Low enzymatic activity haplotypes of the human catechol-O-methyltransferase gene: enrichment for marker SNPs. *PLos One*. 2009;4(4):e5237 PMID: 9365560

PROFESSIONAL PRESENTATIONS

1. The Mobile Phone Solutions for Immunizations (M-SIMU) Trial: A cluster randomized controlled trial in western Kenya. Presented at mHealth Working Group. John Snow Inc. Washington DC. 18 Feb. 2014.

2. The Mobile Phone Solutions for Immunizations Trial (M-SIMU): Sample size and randomization methods. Presented at International Vaccine Access Center (IVAC) at Johns Hopkins University. Baltimore, MD, October 2013.

3. The Mobile Phone Solutions for Immunizations Trial (M-SIMU) in Siaya County: Baseline data, focus group discussions, and study design. Presented at KEMRI/CDC-Kisumu, Kenya. August 2013.

4. Lessons from the field: Improving Childhood Immunization Rates with SMS in Rural Western Kenya. Presented at Johns Hopkins Global mHealth Initiative mHealth Research Seminar Series. Baltimore, MD September 2012.

5. Mobile Phones and Conditional Cash Transfers to Improve Immunization in Kenya. Presented at Center for Global Development, Washington DC, September 2012

6. Using Mobile Money to Improve Healthcare Utilization in Lower Income Countries. Presented as part of the 'Follow the mMoney: How Mobile Money can Improve Public Health' Session at the USAID Global Health Mini-University, Washington DC, September 2012

7. Mu Opioid Receptor: Structural Modeling, Validation, and Application. Presented at 29th Annual Scientific Meeting, American Pain Society, Baltimore, MD, 2010

PEER-REVIEWED ABSTRACTS

1. **Gibson, DG.,** Wakadha, H., Chandir, S., Were, E., Rubin, A., Obor, D., Levine, O., Odhiambo, F., Laserson, K., Feikin D. The feasibility of using mobile-phone based SMS reminders and incentives to promote timely immunization in rural Kenya. Medicine 2.0 5th World Congress on Social Media, Mobile Apps, Internet/Web 2.0, Boston, MA 2012. *Finalist for iMedical Apps and Medicine 2.0 mHealth Research Award*

2. **Gibson, DG** & Feikin D. A systematic review of the literature on distance from health facility and vaccination coverage. 4th Annual The Johns Hopkins Vaccine Initiative Vaccine Day, Baltimore, MD, 2011

3. Hammitt L, Kazungu S, Morpeth SC, Mwarumba S, Bett A, **Gibson DG,** Brent A, Akech DO, Murdoch DR, Nokes DJ, Scott AG. Pneumonia etiology among hospitalized children in Kilifi, Kenya. 4th Annual The Johns Hopkins Vaccine Initiative Vaccine Day, Baltimore, MD, 2011

4. **Gibson, DG,** Dokholyan, N., Setola, V., Ding, F., Yin, S., Serohijos, A., Maixner, B., & Diatchenko, L. Mu Opioid Receptor: Structural Modeling, Validation, and Application. 29th Annual Scientific Meeting, American Pain Society, Baltimore, MD, 2010

5. Nackley A, Conrad M, Slade G, Smith S, **Gibson D**, Kasravi P, Miller V, Lim P, Maixner W, Diatchenko L. Cytokines associated with TMD case status and related intermediate phenotypes. 29th Annual Scientific Meeting, American Pain Society, Baltimore, MD, 2010

6. Smith SB, Miller V, Siddiqi M, **Gibson D**, Arunasalam R, Kasravi P, Neely A, Bair E, Slade G, Maixner W, Diatchenko L. Candidate gene analysis of a persistent pain disorder. NIH Pain Symposium, Bethesda, MD, 2009.

7. Tchivileva IE, Lim PF, , **Gibson D**, Smith S, Diatchenko LB, Maixner W, McLean SA. Propranolol in TMJD treatment. Abstract. American Pain Society, 28th Annual Meeting, San Diego, CA, 2009.

8. Nackley AG, Conrad M, **Gibson D**, Diatchenko L, and Maixner W. Cytokine Profiles Associated with TMD Case Status. Abstract. 7th Annual Conference on Cytokines and Inflammation, San Diego, CA, 2009.

9. Conrad M, Arunasalam R, **Gibson D**, Bair E, Smith S, Slade G, Maixner W, Diatchenko L, and Nackley AG. Proinflammatory Cytokine Profiles Associated with TMD Case Status and Related Intermediate Phenotypes. Abstract. American Pain Society, 27th Annual Meeting, Tampa, FL, 2008.

10. Smith SB, Siddiqi M, Miller V, **Gibson D**, Arunasalam R, Kasravi P, Slade G, Neely A, Bair E, Maixner W, Diatchenko L. Candidate gene analysis reveals genetic pathways associated with a persistent pain disorder. Abstract. American Society for Human Genetics, 58th Annual Meeting, Philadelphia, PA, 2008.

PROFESSIONAL CONTRIBUTIONS

1. **Gibson, DG.** June 2012. Use of mobile phones to increase vaccination and save lives in lower income countries. http://www.imedicalapps.com/2012/06/harnessing-mobile-phone-improve-vaccination-lower-income-countries/

2. **Gibson, DG.** September 2011. From the Field: PCV Research in The Gambia. www.jhsph.edu/research/centers-and-institutes/ivac/IVACBlog/From_the_Field_PCV_research_in_The_Gambia

TEACHING EXPERIENCES

Jan. 2012-
March 2012 Graduate Teaching Assistant, Infectious Disease and Child Survival
Department of International Health, The Johns Hopkins University
Assisted instructors in teaching diverse group of 35-40 clinicians and graduate students. Responsibilities included creating midterm examinations and quizzes; grading examinations and quizzes; providing constructive feedback on final presentations; maintaining course website; addressing student's course concerns
Primary Instructors: Ruth Karron, MD and Andrea Ruff, MD

Oct. 2011-
Dec. **2011** Graduate Teaching Assistant, Vaccine Development and Application
Department of International Health, The Johns Hopkins University
Assisted instructor in teaching over 95 students in concurrent online and on-campus versions of course. Responsibilities included creating midterm and final examinations; grading examinations; maintaining course website; addressing student's course concerns; holding bi-weekly office hours; assisting with bi-monthly live webcasts for online portion of class.
Primary Instructor: Neal Halsey, MD

Aug. 2005-
Dec. 2005 Graduate Student Instructor, Human Neuropsychology course
Department of Psychology, University of Michigan at Ann Arbor
Assisted instructor in teaching an undergraduate level class of over 200 students. Responsibilities included leading bi-weekly discussion groups; creating midterm and final examinations; grading examinations; grading student oral presentations; and addressing student's course concern.
Primary Instructor: Jeffrey Hutsler, PhD

PROFESSIONAL MEMBERSHIPS

- Kenyan National mHealth and eHealth Research Working Group, 2012-present
- Global Health Council, 2009-Present
- *Phi Beta Kappa* National Honor Society, 2003-Present
- Golden Key International Honor Society, 2002-Present
- *Phi Eta Sigma* National Honor Society, 2001- Present

ACHIEVEMENTS/AWARDS

- Best Poster, Vaccine Day at Johns Hopkins University, 2012
- Lipitz Public Health Policy Award- Johns Hopkins University, December 2012
- mHealth Summit Scholarship Award, Johns Hopkins Global mHealth Initiative, November 2012-14
- Finalist for iMedical Apps and Medicine 2.0 mHealth Research Award, September 2012
- Global Health Field Research Award, Johns Hopkins University, April 2012
- Johns Hopkins University- *Clements-Mann Fellowship* for outstanding doctoral student working in vaccine sciences, April 2011

- University of Michigan-Ann Arbor: *Program in Biomedical Sciences Fellowship*, Aug. 2004-May 2006
- State University of New York at Binghamton *Dean's List,* Fall 2000-Spring 2004
- State University of New York at Binghamton: *Binghamton University Scholars Program,* Fall 2000-Spring 2004